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ORTHMANN'S HANDBOOK
OF
GYNÆCOLOGICAL PATHOLOGY.

Ernst Gotlob

ORTHMANN'S HANDBOOK
OF

GYNÆCOLOGICAL PATHOLOGY

FOR PRACTITIONERS AND STUDENTS

TRANSLATED BY

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DR. E. G. ORTHMANN'S PREFACE.

MICROSCOPICAL diagnosis is of the greatest importance to all those who study Diseases of Women. That this is so is evident by the ever-increasing endeavour of those who take their profession seriously, not only to undertake the necessary histological examinations of ordinary cases, but in doubtful ones to be able by this means to form an independent opinion as to their nature. For this purpose two conditions are essential: firstly, a complete mastery of the technique of preparing specimens; and secondly, the art of rightly interpreting the specimens when so prepared. Although the necessary technical skill may be soon acquired without much difficulty, a year of continuous work is at least necessary to attain any proficiency in the proper interpretation of specimens. This can only be obtained by systematically examining and comparing a very large number of preparations. The present work is intended for the assistance and furtherance of these endeavours, and it is hoped that it may be of use not only to those who are beginning the study of microscopical diagnosis, but also to those who are carrying on further investigations in their own practice.

The first portion of the book deals with the most important and modern methods of technique, which are shortly described.

In the second or diagnostic part, the author, in order not to overstep the prescribed limits of the book, has confined himself to the normal histology and pathology of the female sexual organs.

The more uncommon diseases and pathological changes are only briefly dealt with, or altogether omitted, whilst those more frequently met with and which are of special

importance in differential diagnosis are described at length. A short macroscopical sketch in each case precedes the microscopical description.

While even the best illustrations can never adequately take the place of the microscopical examination of the specimens themselves, the author has thought it well to include in the text as many illustrations as possible of some of the most important morbid changes found in gynæcological practice. These may in some measure aid in the recognition and proper interpretation of the various conditions described.

The illustrations, with the exception of fig. 62 and fig. 73, are original; thirty-nine of these have been excellently reproduced by Fraulein Paula Guenther, while the remainder are drawn by the author himself. Some have already appeared in Martin's "Handbook of Diseases of the Female Organs."

The publishers, Messrs. Karger, of Berlin, who first suggested the bringing forward of this work, have spared no pains in the excellence of its production, for which the author tenders them his best thanks.

BERLIN, *October*, 1900.

TRANSLATOR'S PREFACE.

IN venturing to bring forward a translation of Dr. E. G. Orthmann's book,¹ I hope that a want may be supplied for a small work of this sort in the English language, especially as it deals principally with the microscopical appearances of many of the more common diseases of women.

The methods of microscopical technique are shortly described in the first part of the book, while the second is devoted to a description of the histological and pathological changes most commonly found in gynæcological practice.

I feel that there must be many shortcomings in the translation from the German, still the text has been followed with the greatest care, and in this matter I fully acknowledge the valuable assistance of Dr. Max. L. Trechmann.

I am very grateful to Dr. Orthmann not only for giving me permission to translate his book, but also for the use of his plates throughout; these have been sent over by his publishers, Messrs. S. Karger, of Berlin, to whom I also tender my thanks.

Messrs. John Bale, Sons and Danielsson have reproduced the book in English with the greatest care. Dr. J. Abernethy Willett has kindly given me much assistance in revising the proof sheets.

C. HUBERT ROBERTS.

21, WELBECK STREET, W.

January, 1904.

¹ Orthmann, E. G., "Vademecum für Histopathologische Untersuchungen in der Gynækologie." S. Karger, Berlin, 1901.

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GYNÆCOLOGICAL PATHOLOGY.

I.—TECHNIQUE.

(1) Microscopical Instruments.

(a) THE MICROSCOPE.

THE possession of a good microscope is nowadays absolutely indispensable for gynæcological research. The excellence of a microscope depends in the first place on the quality of the lenses, and secondly on the practical arrangement of the stand.

Two objectives and two eye-pieces suffice for most investigations, a stronger and a weaker of each. They should have magnifying powers between 50 — 400 diameters. It is always advisable to use the weaker of the two eye-pieces first.

For bacteriological purposes an oil-immersion lens is also necessary. The stand itself should have a coarse and fine adjustment, and it is convenient to have it so arranged that it can be made to tilt. A concave and a plane mirror serve for illumination, whilst some form of iris diaphragm is required to diminish the light and to cut off the marginal rays. For oil-immersion purposes some form of condenser, such as Abbé's, is essential. It is advisable, finally, to have a revolving nose-piece carrying two or three objectives, as this greatly facilitates their rapid exchange.

A microscope combining all the above conditions,

and which is quite sufficient for most gynæcological purposes, may be obtained of C. Zeiss, of Jena. The following combination is a good one : Stand 4 a. ; eye-pieces 2 and 4 ; objectives AA and DD ; oil-immersion, $\frac{1}{1\frac{1}{2}}$. E. Hartnack, of Potsdam, and E. Leitz, of Wetzlar, also supply very good microscopes.

(b) OTHER INSTRUMENTS.

(1) THE MICROTOME.—A microtome is indispensable for obtaining uniformly thin sections of hardened preparations, and also for cutting frozen sections when a rapid diagnosis of a gynæcological case is of urgent importance ; the sliding microtome made by Schanze, of Leipsig, suffices. With this instrument the knife is moved along a slide by hand, the embedded preparation being fixed in a clamp. Frozen sections can also be cut by means of this machine, freezing being produced by the ether spray. The preparations are gradually raised by means of a micrometer screw according to the thickness of the section required. Further particulars will be given later.

(2) METAL INSTRUMENTS.—The following instruments are usually necessary : a razor with a flat under surface, scalpels, scissors, forceps, section lifters of platinum or German silver. Horn section lifters are very useful. Two or more mounted needles are also required.

(3) GLASS APPARATUS.—Microscope slides, cover-glasses of 0·15—0·20 mm. in thickness, glass dishes with covers, glass rods, pipettes, test tubes, stand with funnels, measure glasses, glass beakers, wash bottle, a plate of black glass and a plate of white porcelain, should be in readiness.

(4) MICROSCOPE LAMPS.—The best light for microscopical purposes is daylight, obtained from white clouds illuminated by the sun ; but as this is not always avail-

able artificial light has to be depended on. For this purpose a gas or paraffin flame is most serviceable, the latter being preferable. It is better to have such light tempered with a globe or cylinder of milk-white glass, or by introducing a pane of blue glass, which is supplied with each microscope, between the mirror and the slide itself.

(2) Examination of Fresh Material.

(a) EXAMINATION OF FLUIDS.

As a rule all that is required in the microscopical examination of fluids is to put a drop of the liquid by means of a pipette or glass rod on to a slide and place a cover-glass over it. In dealing with fluids rich in cells, pus, vaginal secretions, cyst contents, &c., it is necessary to dilute them with normal salt solution (0·6—0·7 per cent.) placed under the cover-glass, the excess of fluid at the edge being removed by means of filter paper. If the fluid to be examined (urine, ascitic fluid, &c.) contains but few cells it may be advisable either to allow it to form a sediment by standing, or to centrifugalise it at once. For the latter purpose a centrifugaliser worked by hand is necessary. This is a more rapid and convenient method, especially when searching for bacteria in fluids. With the examination of blood, urine and sputum, it is assumed that the reader is familiar.

The investigation of aspirated fluids (ascitic fluid, cyst contents, &c.) is of less importance than formerly; nowadays exploratory incision is preferable, for on the one hand it is less dangerous, and on the other it is of much greater value from a diagnostic point of view.

The examination of pus and the secretions of the genital organs is of special importance. For ordinary purposes

it is only necessary to place a drop of the purulent fluid on the slide; but for more minute investigation, and for determining the presence of micro-organisms, dried cover-glass preparations are always used. The recognition of the different varieties of bacteria is considerably facilitated by the use of the various staining methods subsequently described.

In the same way the secretions of the genital tract may be examined, the principal constituents being epithelial cells, squamous epithelium from the vagina, cylindrical epithelial cells from the cervix and uterus, and round cells. From the diagnostic point of view micro-organisms are among the most important constituents. Occasionally other parasites (*Trichomonas vaginalis*) and fungi are found in the vaginal secretion.

The most important bacteria met with in the secretions of the urethra and genital tract are gonococci, streptococci, staphylococci, colon bacilli, and tubercle bacilli. Dried cover-glass preparations are made by placing a small quantity of the fluid to be examined on a carefully cleaned cover-glass. This is done by means of a sterilised platinum loop. The layer of fluid should be as thin as possible; this is best accomplished by laying a second cover-glass on the first, pressing the two lightly together, and then separating them. The cover-glass is now allowed to dry completely in the air, and is then passed two or three times slowly through a spirit or gas flame, the prepared side of the cover-glass being uppermost. After the preparation has been fixed in this way one of the staining methods described below may be employed.

(b) EXAMINATION OF FRESH TISSUES.

(I) SCRAPING AND TEASING METHODS. — These are principally employed in examining preparations of the female genital organs, to determine the constitution of

the larger tumours, the nature and degenerative changes of the tumour cells, as well as that of cells lining cystic cavities.

Scraping Methods.—Scrape a portion of the superficial layer of the inner wall of a cyst with a knife, selecting a part that has not been disturbed by the fingers or in any way damaged. With solid tumours, the freshly cut surface may be similarly treated. Remove the particles to a slide, and add a drop of normal saline solution before examining them under the microscope.

Teasing Methods.—Remove a small portion of the tissue to be examined by means of a knife or scissors; place it upon the slide, and after adding a drop of normal salt solution, tease the piece of tissue into small particles with mounted needles. The teasing is facilitated by immersing the piece of tissue for fifteen or twenty minutes in a freshly prepared 33 per cent. solution of caustic potash. The specimen so prepared should be examined in this solution.

Other reagents used in examining fresh tissues are :—

(1) *Acetic Acid* (2 to 5 per cent. solution).—This renders the nuclei more distinct; it causes the connective tissue to swell up, precipitates the mucin, and dissolves albumen. Fat and elastic fibres remain unaltered.

(2) *Glycerine*.—This serves to clear and preserve the preparation.

(3) *Acetate of Potash* (50 per cent. watery solution).—This acts similarly to glycerine, clearing and preserving the tissues, but it is not as effective.

(4) *Potash and Soda Solutions* (1 to 3 per cent.).—These act by dissociating the tissues; but elastic tissues, fat, amyloid material, pigment, and micro-organisms are unaffected.

(5) *Staining Solutions*.—Dilute iodine solution may be used (1 part Lugol's solution with 4 parts of water); this defines the nuclei more clearly, staining the other

tissues a light yellow colour, whilst amyloid and glycogen-containing tissues are stained dark brown. For the same purpose Löffler's methylene-blue solution may be used (30 parts of a concentrated alcoholic solution of methylene blue, 100 parts of potash solution), [1 in 10,000], or fuchsin acetic acid (2 parts of concentrated alcoholic solution of fuchsin, and 2 parts of glacial acetic acid, to 100 parts of water).

(2) SECTIONS AND SECTION CUTTING.—Whilst scraping and teasing methods do not play a large part in the investigation of gynæcological preparations, the examination of sections is of the greatest importance. This is often necessary when a rapid diagnosis is required to determine the innocency or malignancy of a piece of tissue which has been removed. The razor and knife formerly used in section cutting are now replaced by the freezing microtome. The piece of tissue to be examined may be placed directly in the fresh condition on the freezing plate of the microtome and cut in sections of moderate thickness. It is important in freezing the specimen to be careful not to make it too hard. The sections when cut are removed from the knife by means of a soft camel's-hair brush, and placed in distilled water or normal saline solution, and may be at once examined on the slide. Any of the above-mentioned reagents may be used for clearing or staining them.

Much better sections are obtained by hardening the tissues for a short time before they are cut. For this purpose Müller's fluid or formalin (4 per cent.) answer well, the specimen being allowed to lie in the fluid for half an hour to an hour; they must then be thoroughly washed in water. The piece of tissue to be frozen should not be more than 0·3 to 0·5 cm. in thickness.

Sections prepared in this way make excellent permanent preparations, and can be subjected to various staining methods. They are removed from the dis-

tilled water or salt solution, and placed by means of a section lifter or spatula, first into a 70 per cent. and then a 96 per cent. alcohol. It is advisable while doing this to keep the section on the section lifter until it has been in contact with the 96 per cent. alcohol for some time. It is also important to place a drop of alcohol by means of a glass rod on the centre of the section on the section lifter, thereby avoiding the tendency which the section often has to roll itself up.

Pick has described a specially rapid method of preparing permanent preparations from fresh tissues as follows :—

- (1) Prepare the frozen sections.
- (2) Place the sections in 4 per cent. formalin solution (made with boiled water) for fifteen seconds.
- (3) Stain with formalin - alum - carmine (Grenacher's alum-carmine 100 parts, formalin 10 parts) for two to three minutes.
- (4) Wash in water for half a minute.
- (5) Eighty per cent. alcohol : half a minute.
- (6) Absolute alcohol : ten seconds.
- (7) Carbol-xylol : half a minute.
- (8) Mount in Canada balsam.

These methods are not suitable for very soft and friable tissues, as the fixation takes place after freezing, and the section thus easily falls to pieces. This may be avoided by Kiefer's method, which is not only applicable to all tissues, but it also allows of collective staining methods, and even the examination of bacteria, &c. It requires, however, rather more time. The technique is as follows :—

- (1) Place the specimen, without previous washing, in concentrated formalin for six to eight hours. By this means the adherent blood, especially with very soft tissues acts like a cement, preventing the section from falling to pieces and does not in any way spoil its microscopical appearance.

- (2) Wash in water six to eight hours.
- (3) Cut with freezing microtome.
- (4) Eighty per cent alcohol : one minute.
- (5) Absolute alcohol : half a minute.
- (6) Stain with hæmatoxylin and eosin, &c., and then proceed as with celloidin sections (*vide infra*).

In Gebhard's modification of this method, the tissue is first washed in water, placed for two or more hours in absolute alcohol, and then for a similar length of time in formalin.

Preparations hardened in alcohol may also be cut with the freezing microtome, but the alcohol must first be entirely removed by thoroughly washing in water. Specimens containing alcohol of course will not freeze.

In cases where a rapid diagnosis is not required it is far better to harden and embed the tissue carefully by one of the following methods:—

(3) Methods of Hardening Preparations.

For special microscopical examinations it is very important not to attempt to harden too large a piece of tissue. Small pieces excised or scraped away are easily dealt with; but with large tumours or organs totally extirpated (uterus, tubes, ovaries, &c.), it is best to cut out small dice-shaped pieces or slices from the fresh specimen. In the case of hollow viscera the section is best made perpendicular to the lumen. The particular tissue should be placed as soon as possible after removal in one or other of the following hardening fluids:—

(1) *Müller's Fluid* :—

Potassium bichromate	2.0 parts.
Sodium sulphate	1.0 „
Water	100.0 „

Small pieces are sufficiently hardened in this fluid in eight to fourteen days. During the first few days the fluid should be changed every other day.

(2) *Zenker's Fluid* :—

Corrosive sublimate	5·0 parts.
Glacial acetic acid	5·0 „
Müller's fluid	100·0 „

It is advisable to add the glacial acetic acid just before the fluid is required. Small portions of tissue require only twelve to twenty-four hours in this fluid.

(3) *Formalin* (4 per cent. solution). — Concentrated formalin consists of a 40 per cent. solution of formaldehyde, so 10 parts of this are required to 100 parts of water. For hardening moderate sized pieces of tissue twelve to twenty-four hours suffice. A longer period is not detrimental.

(4) *Flemming's Mixture* :—

Osmic acid	0·4 parts.
Chromic acid	0·75 „
Acetic acid	5·0 „
Distilled water	100·0 „

Tissues must be allowed to lie in this fluid from 12 to 48 hours, according to size.

(5) *Alcohol* (70 to 96 per cent.)—Preparations to be examined for bacteria may be placed straight into absolute alcohol.

Tissues which have been hardened in Nos. 1 to 4 of the above-mentioned fluids must be thoroughly washed, if possible, in running water, or at any rate in several changes of water, before further treatment; they must then be placed in 80 per cent., 96 per cent., and finally absolute alcohol.

The Kaiserling-Pick method is specially recommended for preserving the natural colour of morbid anatomical preparations :—

(1) Place the specimen in a solution of formalin 20 parts, artificial Carlsbad salts (German Pharmacopœia) 20 parts, and distilled water 400 parts, for thirty-six to forty-eight hours.

(2) Eighty-five per cent. alcohol for five to six hours.

(3) Put up permanently in—

Acetate of potash	270 parts.
Glycerine	540 „
Water	900 „

(4) **Embedding of Tissues.**

The aim of embedding methods is to impart to soft preparations, and more especially those containing a cavity, such a consistency as will allow them to be easily and safely cut with a microtome, without injuring the specimen or displacing its contents.

The principle of embedding consists in saturating the preparation with a fluid medium which later is allowed to set. The most convenient embedding media are those which after the section is prepared do not again require to be removed from it. Previous embedding is absolutely essential when a large number of serial sections is required. The most useful embedding media are celloidin and paraffin.

(a) CELLOIDIN EMBEDDING.

Schering's celloidin, which is sold in tablets, is first cut into small cubes, and then dissolved in equal parts of absolute alcohol and ether. The solution should be of a thick syrupy consistency. To get a thinner solution more ether and alcohol should be added. For embedding purposes a thick and a thin solution are required.

The tissues hardened in the manner above described (page 8) must first of all be completely freed from water by a lengthened immersion in absolute alcohol. They are then placed for twenty-four hours in a mixture of equal parts of alcohol and ether. After this, the tissues are placed for two to four days in the thinner, and then for the same period in the thicker, solution of celloidin.

For fixing celloidin preparations, Orthmann's method of using small square or oval blocks of wood which fit on to the microtome clamp will be found very useful. Poplar wood is very suitable for the purpose, as it possesses the great advantage of being unaffected by spirit, and contains no material which might alter or injure the tissues to be examined.

The pieces of tissue are removed by means of forceps from the thicker celloidin and placed on the wooden block, previously moistened with the alcohol and the ether solution. Then the thicker celloidin solution is poured over the specimen until it is completely covered. The celloidin is then allowed to dry slowly under a glass bell jar for half an hour to an hour, until the surface is so far set that it no longer sticks to the finger. The block is then placed in a wide vessel containing 80 per cent. alcohol. Care must be observed that the preparation is on the under surface of the block. After a time, the wooden block sinks to the bottom of the alcohol. It will be firm enough for cutting in about one to two days. Blocks may be preserved in 80 per cent. alcohol and retain their normal capacity for staining for as long a time as one to two years.

In cutting celloidin sections with the microtome, it is important that the knife be placed as obliquely as possible, so that the whole length of the incision goes through the preparation; also, the knife as well as the specimen must be kept constantly moist with 80 per cent. alcohol. The sections are removed from the knife by means of a camel's-hair brush to a small glass dish containing 80 per cent. alcohol, and then stained.

(b) PARAFFIN EMBEDDING.

The preparations, having been completely dehydrated by absolute alcohol, are first of all placed for four to twelve hours in xylol, then for four hours in a mixture

of xylol and paraffin in equal parts, and lastly for four hours in pure paraffin, the melting point of which is about 50° C. The last two procedures must be conducted in a paraffin oven at 50° C. Then the tissue with the fluid paraffin is poured into a small cardboard or metal mould, or into a glass dish, and brought into the proper position with warmed needles. The paraffin may be fixed by placing it into, or upon, cold water. When the paraffin is sufficiently set, the preparation is taken out of the mould and the superfluous paraffin cut away. It is then fixed on a wooden block by means of warmed needles, and cut with a dry knife. Preparations embedded in paraffin may be preserved dry for a very long period.

The further treatment of the sections consists in first removing the paraffin by placing them in xylol, thence transferring them to absolute alcohol, then to water, and finally staining them. With very fragile tissues it is advisable to place the paraffin sections direct on to a slide covered with warm water, the superfluous water being allowed to run off and the rest removed by blotting paper. The slide is then placed for some hours in the thermostatic oven at 37° C. Finally the slide with the preparation is placed in xylol to completely remove the paraffin, and then further treated as above described.

Although the production of a large number of serial sections (ribbon sections) is a somewhat difficult matter with the celloidin method, with paraffin this will be found much simpler. The details on this point should be looked up in special text-books dealing with microscopical technique.

(5) Staining Technique.

(a) STAINING OF MICRO-ORGANISMS.

In staining micro-organisms a distinction must be made between cover-glass preparations and sections.

The staining reagents are practically the same for both, but the after-treatment is somewhat different.

(1) COVER-GLASS PREPARATIONS.—The three principal dyes used in staining micro-organisms are methylene blue, gentian violet, and fuchsin. The following formulæ will be found useful:—

(1) *Methylene Blue.*

(a) In concentrated aqueous solution.

(b) Löffler's methylene blue.

(i.) Concentrated alcoholic solution of methylene blue, 30 parts.

(ii.) Potash (1 in 10,000), 100 parts.

(2) *Gentian Violet.*

(a) In concentrated watery solution.

(b) Anilin water solution.

(i.) Anilin oil, 1 part; distilled water, 20 parts. Well shaken and then filtered.

(ii.) To the anilin water a concentrated alcoholic solution of gentian violet is then added until the solution becomes opaque. This is best done in a test tube and should always be freshly prepared.

(3) *Fuchsin.*

(a) In concentrated alcoholic solution.

(b) Carbol fuchsin.

Fuchsin 1 part.

Absolute alcohol 10 parts.

Pure carbolic acid .. 5 „

Distilled water 100 „

The staining of cover-glass specimens prepared in the way described above is most quickly and practically carried out by fixing the cover-glass in a pair of Cornet's forceps and applying two to three drops of

the required staining solution by means of a glass rod, care being taken that the surface is completely covered with the stain. Hold the cover-glass with the stain for a minute over the flame of a spirit lamp (at a hand's-breadth distance), wash the superfluous stain away in a beaker of water or by means of a wash bottle, allow the preparation to dry completely, and mount in Canada balsam.

The simplest way of staining is with a concentrated watery solution of methylene blue. This suffices for the various pus cocci, gonococci, &c.

With regard to differential diagnosis, Gram's method of staining is very important. It is carried out in the following manner:—

(1) Stain the cover-glass preparation with anilin gentian violet for three to five minutes.

(2) Place it in Lugol's solution (iodine, 1 part; iodide of potassium, 2 parts; distilled water, 300 parts) for one to two minutes.

(3) Then in absolute alcohol till the preparation, which at first is almost black, appears of a light grey colour.

(4) Mount in Canada balsam.

Only certain varieties of micro-organisms retain the stain by this method, the most important being *Streptococcus pyogenes*, the *Streptococcus* of erysipelas, *Staphylococcus pyogenes*, *albus*, *areus*, *citreus*, and *flavus*. Anthrax bacilli, diphtheria bacilli, tubercle bacilli, leprosy bacilli, tetanus bacilli, and Fränkel's pneumonia-diplococci, also stain by Gram's method.

On the contrary, the following become decolourised: Gonococci, *bacterium coli commune*, typhoid bacilli, and cholera bacilli. Unstained bacteria which lose the stain in this method may, however, be counter-stained with a fuchsin solution (concentrated alcoholic solution of fuchsin, 3 to 5 drops; distilled water, 30 parts). Thus, in a mixture of bacteria, gonococci which are

decolourised by Gram's method become stained red, whilst certain other bacteria are stained dark blue.

The staining of tubercle bacilli is of importance; the following is probably one of the best methods:—

(1) Stain the cover-glass preparation with carbolfuchsin solution (see above, page 13), hold over the flame for three to five minutes.

(2) Place in hydrochloric acid alcohol (pure hydrochloric acid, 1 part; alcohol, 70 per cent., distilled water, 100 parts) until no more red colour is given off.

(3) Wash in water.

(4) Counterstain in concentrated watery methylene blue solution for one to two minutes.

(5) Wash in water.

(6) Dry.

(7) Mount in Canada balsam.

By this means tubercle bacilli are stained red, while other bacteria and the tissues are stained blue.

(2) STAINING BACTERIA IN SECTIONS.—In order to demonstrate micro-organisms in the tissues, small pieces as fresh as possible should at once be placed in absolute alcohol to harden. They can then be embedded in celloidin.

The sections obtained with the microtome are stained by one of the above-mentioned methods. They should, however, be allowed to remain rather longer in the staining fluid than ordinary dry cover-glass preparations.

It is sometimes a good plan to accelerate the process by warming the staining solution in a watch-glass over a spirit flame: the right degree of heat may be judged by steam arising from the surface of the stain, or by the presence of small bubbles.

In the examination of pyogenic organisms and gonococci, it will be sufficient to leave the sections for a quarter to half an hour in a concentrated watery solution of methylene blue, which may be slightly warmed.

The sections are then washed for a moment in distilled water and are immediately placed in absolute alcohol for a half to one minute. The sections are then cleared in origanum oil or carbol-xylol (pure carbolic acid 1 part, xylol 3 parts) and mounted in Canada balsam. By this method gonococci in sections may be easily demonstrated. Gram's method, as described above, may likewise be used for section staining.

Tubercle bacilli may be demonstrated by carbol-fuchsin by the method already mentioned, the preparations remaining up to twenty-four hours in the staining solution. After decolourising with hydrochloric alcohol, washing and counter-staining in concentrated watery methylene blue solution, the sections are rinsed in water, dehydrated for half to one minute in absolute alcohol, then cleared in origanum oil or carbol-xylol, and mounted in Canada balsam.

(b) SECTION STAINING.

Only those particular stains and staining methods which are important in gynæcological work will here be dealt with. The most useful stains are hæmatoxylin and carmine. Böhmer's or Ehrlich's hæmatoxylin is very serviceable, and can easily be procured made up ready for use. If necessary or desirable they can be prepared according to the following formulæ:—

(1) *Böhmer's Hæmatoxylin*:—

Hæmatoxylin	1 part.
Absolute alcohol	30 parts.

To this solution is added an aqueous 1 per cent. solution of alum, drop by drop, till a violet tint appears. After some days (eight to ten), during which the stain should be freely exposed to light, the solution becomes blue. The longer the solution stands the more intense does its staining power become.

(2) *Ehrlich's Hæmatoxylin* :—

Hæmatoxylin	2 parts.
Absolute alcohol	100 „
Alum	2 „
Distilled water	100 „
Glycerine	100 „
Glacial acetic acid	2 „

This solution becomes fit for use after it has stood two to three weeks exposed to light.

All staining solutions should be filtered immediately before use.

Section staining with hæmatoxylin is carried out in the following manner :—

(1) Hæmatoxylin, ten to fifteen minutes.

(2) Hydrochloric alcohol (1 part hydrochloric acid to 100 parts of 70 per cent. alcohol) one to three minutes.

(3) Wash in distilled water, to which a few drops of ammonia have been added (five to six parts to 50 parts of water).

(4) Wash in distilled water.

(5) Absolute alcohol, two to three minutes.

(6) Origanum oil, two to three minutes.

(7) Canada balsam.

Very beautiful double staining may be obtained with hæmatoxylin preparations by adding to the alcohol which is used for dehydration eight to ten drops of eosin (concentrated alcoholic solution), or five to six drops of picric acid (concentrated aqueous solution).

Double staining by van Gieson's method is also very useful. By this means the nuclei are stained a brownish-red tint, connective tissue bright red, and the muscular bundles orange-red.

Van Gieson's method is as follows :—

(1) Hæmatoxylin, two to twenty-four hours.

(2) Wash in water, five to ten minutes.

(3) Picric acid fuchsin, three to five minutes (concen-

trated watery picric acid solution 2 parts, concentrated watery acid fuchsin solution 1 part. The stain should appear deep red).

(4) Wash in water, half to one minute.

(5) Absolute alcohol.

(6) Origanum oil.

(7) Mount in Canada balsam.

Of the carmine stains, probably alum carmine is most satisfactory. It is prepared by boiling 2 to 3 grammes of carmine with 100 grammes of a 5 per cent. alum solution, for half an hour to an hour. After it has cooled this is filtered. Sections can then be stained in the following way :—

(1) Alum carmine, ten minutes to one hour.

(2) Wash in water.

(3) Absolute alcohol, one to three minutes.

(4) Origanum oil.

(5) Canada balsam.

With carmine staining it is almost impossible to over-stain the sections.

Preparations which have been hardened in Flemming's solution (page 9) may be stained with saffranin; this method is most useful in demonstrating segmentation of the nuclei. It is as follows :—

(1) One per cent. watery solution of saffranin, from half an hour to twenty-four hours.

(2) Wash in water for a few seconds.

(3) Absolute alcohol 50 parts, hydrochloric alcohol (1 per cent.) 5 to 10 parts.

(4) Absolute alcohol, till the sections appear of a bright brownish-red colour.

(5) Origanum oil.

(6) Canada balsam.

In conclusion, the most useful reagents and staining materials are given below :—

(1) *Reagents, &c.* — Glacial acetic acid, glycerine,

normal saline solution (0·6 per cent.), acetate of potash, caustic potash, formaldehyde, absolute alcohol, Müller's fluid, ether, celloidin, origanum oil, Canada balsam, Lugol's solution, hydrochloric acid, carbolic acid, aniline oil, alum, distilled water.

(2) *Staining Materials*.—Methylene blue, gentian violet, fuchsin, acid fuchsin, hæmatoxylin, eosin, picric acid, carmine, saffranin.

II.—DIAGNOSIS.

A.—DISEASES OF THE VULVA.

(1) Inflammations and Infective Granulomata.

(a) INFLAMMATION.

In dealing with inflammation of the vulva it is of the greatest importance if possible to determine its etiology from the character of the discharge.

Most inflammatory changes of the vulva are not primary, but result from diseases of the urethra, vagina, or uterus. These are accompanied by redness and swelling of the vulva as well as by a thick whitish muco-purulent or purulent discharge. The latter often contains degenerate epithelial cells and leucocytes.

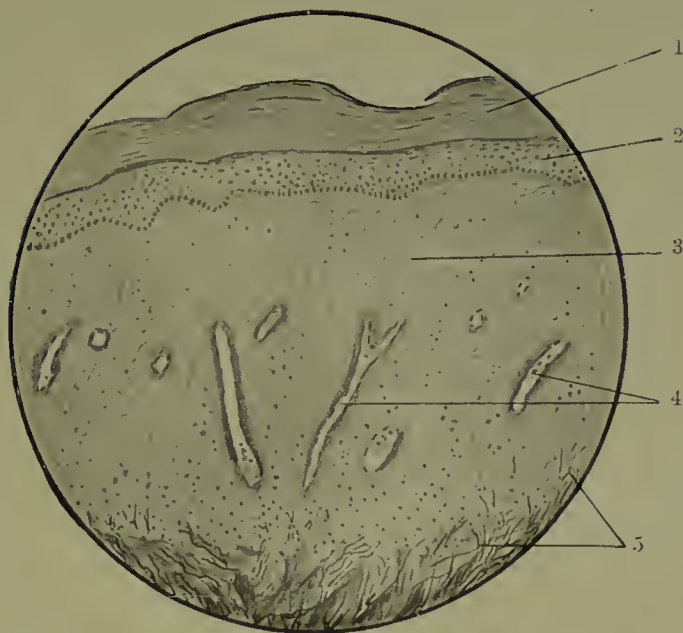
In examining such discharges, the presence of micro-organisms is of great importance. Those most usually found are gonococci, pus cocci, streptococci, and staphylococci. Diphtheria bacilli, tubercle bacilli, bacterium coli, as well as various saprophytes (*leptothrix*, *oidium albicans*, &c.), are of much rarer occurrence.

As a result of vulval inflammation various forms of dermatitis are frequently met with (eczema, erythema, herpes, pruritus, impetigo, acne, furuncle, gangrene, &c.). Another sequela, occurring especially in connection with gonorrhœal vulvitis, is suppuration of the glands of Bartholin. Gonococci and other pus cocci may be easily demonstrated in the discharge.

A special form of disease, which apparently originates as the result of inflammation, is known as kraurosis vulvæ. In the final stages of this condition there is

FIG. 1.

KRAUROSIS VULVÆ (ATROPHIC STAGE).



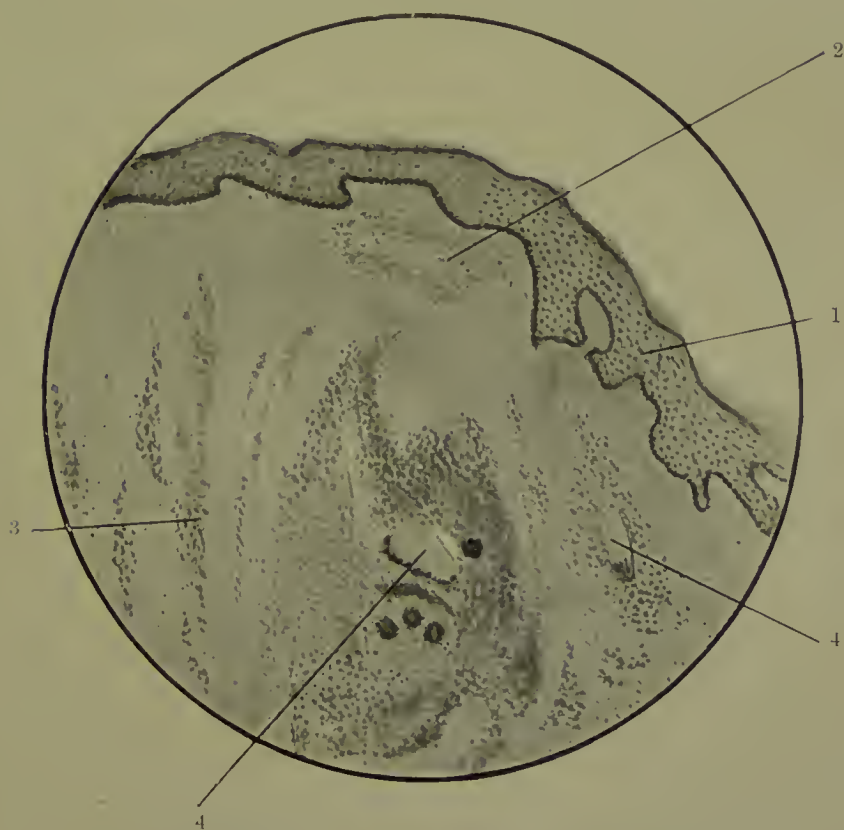
1. Stratum corneum.
2. Stratum mucosum.
3. Corium, showing shrinking and sclerosis of the papillæ.

4. Vessels.
5. Limit of elastic fibres.

(Orcein staining.)

FIG. 2.

TUBERCULOSIS VULVÆ.



1. Superficial squamous epithelial layers.
2. Focus of small-celled infiltration under the epithelium.
3. Patch of small-celled infiltration in the corium.
4. Tubercle nodule with epithelioid and giant-cells.

(Fuchsin methylene-blue staining.)

shrivelling of the labia and clitoris, which have a whitish, dry appearance. A curious brittleness of the surrounding skin is often seen as well. Excised portions are best hardened in formalin and alcohol. Under the microscope both an hypertrophic and an atrophic stage can be distinguished. In the former a small-celled infiltration is found in the corium, with hyperplasia of the connective tissue. In the second or atrophic stage, a marked shrinking of the stratum mucosum sets in with simultaneous flattening and ultimate disappearance of the papillæ. The corium is no longer wavy, but stretched and sclerosed, and has a peculiar shiny white appearance. Isolated patches of small-celled infiltration are seen especially in the neighbourhood of the vessels, which are scanty.

A characteristic feature of the disease is that the elastic tissue (Orcein staining*) in the diseased areas, completely disappears (fig. 1). Carcinoma is sometimes associated with kraurosis vulvæ.

(b) INFECTIVE GRANULOMATA.

The various syphilitic affections of the vulva scarcely afford a subject for microscopical investigation, but tuberculous lesions, though rare, are important. These usually occur in the form of ulceration (lupus vulvæ, &c.). In such cases the edges of the ulcer are thickened, irregular, and undermined, whilst the base is covered with greyish-red granulations, in which, here and there

* Method of staining with Orcein: (1) Orcein solution (orcein 1·0 part, absolute alcohol 80·0 parts, distilled water 40·0 parts, hydrochloric acid 40 drops), six to twenty-four hours; (2) one per cent. hydrochloric alcohol, two to three minutes; (3) absolute alcohol; (4) origanum oil; (5) Canada balsam. A counterstain with alum carmine is recommended. For this purpose the sections should be removed from the hydrochloric alcohol into water, and then stained with carmine (p. 18).

miliary tubercles are to be seen. In the neighbourhood of the ulcers elephantiasis-like growths and polypoid formations are not infrequently found. In examining tissues of this nature, it is best to harden them in absolute alcohol, as this method allows of further investigation for tubercle bacilli.

Microscopically, in those parts where the disease is most advanced the surface is covered by granulation tissue, in which characteristic tuberculous nodules occur either singly or in groups. The tuberculous nodules consist mainly of epithelial and round cells, and usually contain one or more giant cells with marginal nuclei. Occasionally tubercle bacilli may be found in their interior, but they also occur outside the giant cells. The tuberculous nodules in the granulation tissue are very evident by their small staining capacity as compared with the surrounding cells.

Isolated tuberculous nodules are also met with in the corium in places which are still covered with normal surface epithelium (fig. 2). Caseation may be seen beginning in the centre of such nodules, and occasionally tubercle bacilli can also be demonstrated in them.

(2) New Growths.

(a) INNOCENT NEW GROWTHS.

(1) CYSTS.—Cystic growths may affect the labia majora and minora, as well as the hymen; the most common are cysts of Bartholin's glands. These usually contain a thin serous, or else a thick mucoid fluid of a yellowish or brownish colour. They are lined by tall, cylindrical epithelium and have a thin capsule of fibrous tissue.

Besides these, other varieties of retention cysts occur; they arise usually from sebaceous glands and possess the characters of skin atheromata.

FIG. 3.

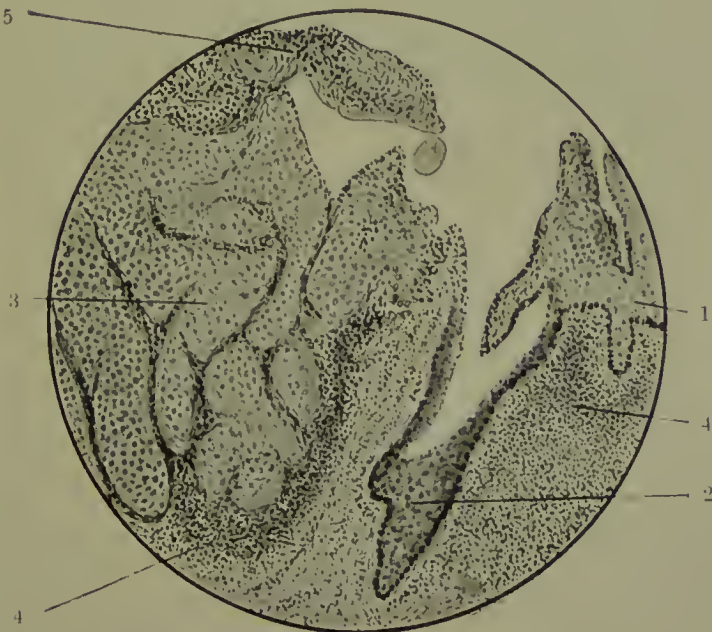
WARTS FROM THE VAGINA (CONDYLOMATA ACUMINATA).



- 1 Enormously thickened, scaly, epithelial layers.
 - 2 Thinned-out papilla, infiltrated with small round cells.
- (Hematoxylin-eosin stain.)

FIG. 4.

CARCINOMA OF THE VAGINA.



1. Proliferating squamous epithelial layer.
2. Epithelial cones extending into the deeper parts.
3. Epithelial nests and cones, with delicate connective tissue stroma.
4. Small-celled infiltration at the growing edge of the carcinoma.

(Hematoxylin-eosin stain.)

Dermoid cysts of the vulva are also found containing atheromatous material and hair. They are lined with flattened epithelium.

Cysts formed by the adhesion of folds of skin are very rare. Lymphatic cysts, hydrocele of the round ligament, cysts of Gartner's ducts or the Wolffian bodies, have also been observed.

(2) WARTS (*Condylomata Acuminata*).—These may occur singly, or in such large numbers that the labia are completely covered by them, the tumour sometimes resembling a papillomatous new growth. They occur usually in connection with gonorrhœa and pregnancy, and may extend into the vagina. They consist principally of an hypertrophy of the epithelial and papillary layers of the true skin.

Under the microscope (fig. 3) the horny and mucous layers are extraordinarily thickened, beneath which the thin papillæ are increased in height, and branch repeatedly. The papillæ contain numerous capillary vessels and scattered collections of small round cells.

(3) ELEPHANTIASIS VULVÆ.—Elephantiasis of the vulva consists chiefly of an inflammatory hypertrophy of the connective tissue. It occurs on one or both sides, and affects the labia majora, labia minora, or the clitoris, forming swellings of considerable size. These may have either a smooth surface (*Elephantiasis glabra*), or they may be rough and nodular (*Elephantiasis verrucosa s. tuberosa*).

Histologically, the growth consists of œdematous fibrous tissue which often contains dilated lymphatic spaces. Clusters of small round cells occur in the neighbourhood of the vessels, and at times the papillæ and epithelial layers of the skin are markedly hypertrophied.

(4) CONNECTIVE TISSUE TUMOURS.—Innocent connective tissue tumours of the vulva are extremely un-

common. They include fibromata and fibro-myomata, which may sometimes attain a considerable size. Lipomata of the mons veneris or labia majora, angiomata, enchondromata, and neuromata, occur very rarely.

(b) MALIGNANT TUMOURS.

(1) CARCINOMA.—Carcinoma arises either from the clitoris, the glands of Bartholin, or more usually from the mucous membrane of the vulva, at its junction with the vaginal orifice. Carcinoma affecting the glands of Bartholin is very rare, and generally takes the form of an alveolar cylindrical-celled cancer.

The most common variety met with is squamous-celled cancer, identical with carcinoma of the skin occurring in other parts. Squamous carcinoma appears either in a papillary form, the surface of which is frequently ulcerated, or as a hollowed-out ulcer with thickened edges. Small whitish-yellow nodules can usually be seen covering the surface of the ulcer; these represent epithelial plugs, and can easily be squeezed out by pressure. The growth rarely spreads very widely over the vaginal mucosa, though carcinoma of the clitoris may extend to the urethral orifice. The inguinal glands are only affected late in the disease, and in old people this may be deferred for a very long time.

Microscopically, epithelial processes are first seen extending between the papillæ, and in the end they lengthen and ramify into the deeper parts. In the neighbourhood of the epithelial processes and cell-islands, more or less well marked round-celled infiltration is observed. Abundant cell-nests are to be seen in the epithelial processes.

After existing for some time the surface of the ulcer disintegrates, and becomes covered by granulation tissue, while the deeper layers still exhibit a true picture of horny cancer (Hornkrebs).

(2) SARCOMA.—Sarcoma of the vulva occurs much less frequently than carcinoma, but may attain a considerable size. Round and spindle-celled sarcomata are found, while pigmented tumours (melanotic sarcomata) are not very uncommon. Similar abnormal pigmentation of a carcinomatous growth (melanotic carcinoma) has been observed.

B.—DISEASES OF THE VAGINA.

(1) **Inflammation and Infective Granulomata.**

(a) INFLAMMATION.

What has already been said with regard to the character of the secretions in inflammation of the vulva applies also to inflammatory changes in the vagina. Etiologically, the majority of such inflammations depend on infection, but traumatism is responsible for some varieties.

Three forms of Colpitis, or inflammation of the vagina, can be distinguished, viz., catarrhal, ulcerative and emphysematous.

(1) *Catarrhal Colpitis*. — This is characterised by a marked increase of secretion together with redness and swelling of the mucous membrane of the vagina, while in the later stages circumscribed reddened patches often occur. These patches are due to shedding of the superficial epithelium, and to consequent exposure of the underlying reddened and congested papillæ. In gonorrhœal infection the mucous membrane often appears covered with little nodules, which correspond to the inflamed and thickened papillæ, these give a granular appearance to the vagina (granular colpitis). In old women, the eroded patches on the mucous membrane sometimes lead to adhesions (senile adhesive colpitis) which may give rise to considerable stenosis of the vagina.

(2) *Ulcerative Colpitis*.—In this form extensive ulceration may occur, either due to the fusion of several eroded patches following a catarrhal inflammation, or else to traumatic causes. Among the latter are ulcers due to the pressure of badly-fitting or long-neglected pessaries, and those caused by extensive prolapse of the vagina. Such ulcers present most various forms, but generally have raised somewhat thickened edges. The mucous membrane may become extensively undermined, and large portions may sometimes be cast off (*colpitis exfoliativa* s. *dissecans*).

In puerperal infection, a phlegmonous colpitis or paracolpitis may lead to complete shedding of the vaginal mucous membrane in the form of a cylindrical cast.

Histologically, in all the above-mentioned varieties there is, in the early stages, a circumscribed or diffuse infiltration of round cells beneath the squamous layer.

In the circumscribed form, the infiltration may extend to several adjacent papillæ, pushing up the epithelial layers, thus giving rise to so-called granular colpitis. The blood-vessels in the neighbourhood of the infiltrated areas are increased in number and are much injected. In the further course of the inflammatory changes the superficial epithelial layers overlying the infiltrated spots become thinned, and may finally disappear altogether, so that the inflamed papillæ lie exposed on the surface.

The inflammation very rarely extends to the deep layers of the cutis, but here and there collections of round cells may be found following the course of the vessels.

Such ulcerative processes lead to the formation of a granulating surface of variable size and shape, which after destruction of the epithelial and papillary layers may extend deeply into the underlying tissues. The surface is sometimes covered by a layer of fibrinous exudation, beneath which is a connective tissue stratum

infiltrated by small round cells and traversed by innumerable deeply injected capillaries.

At the edge of the ulcer, the surface epithelium is usually normal in appearance and quite healthy. When healing commences, thin layers of epithelium may be seen to extend from the edges and to grow over the surface of the ulcer.

Numerous bacteria are to be found within the inflamed tissues, usually corresponding with those found in the vagina. Of these the gonococcus is the most difficult to demonstrate. [The best section stain for this purpose is the concentrated aqueous solution of methylene blue.]

(3) *Emphysematous or Cystic Colpitis*.—This usually occurs in connection with pregnancy, and is characterised by the occurrence of numerous small gas-containing vesicles immediately under the surface epithelium. The vesicles give rise to projections of the mucous membrane which vary in size, and which disappear on pressure with the finger. They are produced by a gas-forming bacillus.

Under the microscope, the sub-epithelial connective tissue is found to be studded with numerous cavities, which for the most part follow the course of the blood-vessels. The cysts are occasionally lined with endothelium. This endothelial lining is sometimes seen to be undergoing proliferative changes and transformation into giant cells.

Some cavities lined by endothelium apparently arise in connection with lymph vessels, whilst others give the impression of being merely interstices in the tissues themselves. The vaginal mucous membrane in the neighbourhood of the cavities is usually reddened as a result of increased vascularity, and is accompanied by small-celled infiltration. The gas contained in the cavities has been proved to be trimethylamin.

(b) INFECTIVE GRANULOMATA.

Syphilitic affections of the vagina are rare. Tuberculous disease is likewise uncommon, though of more importance for purposes of diagnosis. Tubercle of the vagina may be primary or secondary. It occurs chiefly in the form of superficial ulceration which has an uneven jagged edge, and a greyish surface.

Microscopical examination shows characteristic tuberculous changes in such cases—granulation tissue, with nodules containing giant cells. The number of tubercle bacilli found is usually very small.

(2) Tumours of the Vagina.

(a) INNOCENT NEW GROWTHS.

(1) CYSTS.—Vaginal cysts usually occur on the anterior or lateral walls of the vagina, less frequently on the posterior. They are not generally of large size, seldom exceeding that of a walnut. Their structure and contents differ according to their origin. Most of the small cysts arise from glands, and are really retention cysts; they are, as a rule, lined by a low cylindrical epithelium, which, however, does not maintain a uniform character, for in some cases the cysts contain a many-layered squamous epithelium.

The walls usually consist of dense connective tissue, in which unstriated muscular fibres may be found.

Vaginal cysts may also arise from the remains of Gartner's duct; these usually occur on the anterior or lateral walls of the vagina, and may extend for a considerable distance into the parametrium. Their epithelial lining is not always uniform in character, cylindrical epithelium usually preponderates. Occasionally, invaginations of the walls of these cysts occur, in which unstriated muscular fibres are not uncommon.

Finally, simple lymphectatic cysts are found in the vagina, lined with flattened epithelium.

The fluid found in vaginal cysts may be either clear or turbid, or may be mucoid or atheromatous in character.

(2) WARTS (*Condylomata Acuminata*).—Warts sometimes occur in extraordinary numbers in the vagina, and may extend to the external os uteri. Their histological structure is identical with those occurring in the vulva (see p. 23).

(3) CONNECTIVE TISSUE TUMOURS.—Benign growths of this nature are very rarely met with in the vagina. Mucous polypi are sometimes found having a broad pedicle; they are covered with pavement epithelium, and glandular cavities are found in their interior. The ground substance of these tumours is composed of fibrous connective tissue.

Fibromata and fibro-myomata also occur, and are often pedunculated; they generally grow from the anterior vaginal wall. They are composed of fibrous connective tissue mingled with scanty unstriped muscular bundles. Lipomata occurring in the vagina are very rare.

(b) MALIGNANT NEW GROWTHS.

(1) CARCINOMA.—Carcinoma of the vagina may be primary or secondary. Two forms of primary cancer are to be recognised—the *circumscribed* or papillary (Hornkrebs), which usually occurs on the posterior vaginal wall; and the *diffuse* or annular carcinomatous infiltration. The latter may affect the whole vaginal tube, causing widespread ulceration and destruction. Secondary carcinoma of the vagina usually results by extension of the growth from the uterus, bladder, or rectum.

Under the microscope in the early stages of cancer of

the vagina, an abnormal proliferation of the squamous epithelium is seen, which extends between the papillæ into the deeper layers in the form of downward-growing cone-like processes of cells. The shape and arrangement of the cells may remain at first unaltered. An active small round-celled infiltration usually occurs in the neighbourhood of these rapidly proliferating cone-like cancer processes (fig. 4).

As the disease progresses, the superficial layer of epithelium is lost, the abnormally proliferating squamous cells taking its place. Later, the surface of the cancerous area is covered by a thin layer of granulation tissue or a deposit of fibrin. In the interior of the cell-nests and cones, cancrioid epithelial pearls frequently occur. This is characteristic of horny cancer (Hornkrebs).

As the majority of secondary carcinomata of the vagina extend from the vaginal portion of the cervix to the vagina, they present a similar structure. Metastatic tumours in the vagina arising from primary carcinoma of the cervix or body, present the same structure as the primary tumour, viz., adeno-carcinoma.

Metastatic deposits of syncytioma malignum are sometimes met with in the vagina, the primary disease beginning in the body of the uterus or Fallopian tubes. The peculiar structure of this form of new growth will be dealt with later (see p. 65).

(2) SARCOMA.—Sarcoma of the vagina occurring in children must be distinguished from that affecting the adult. The former is usually congenital, and is characterised by its papillary or grape-like appearance. It occurs commonly on the anterior wall.

Sarcoma in the adult appears either as a circumscribed, nodular tumour, or in the form of a diffuse ring-like infiltration of the whole vaginal wall. It may occur either on the anterior or posterior aspect of the vagina. In its further progress the surface of the tumour may undergo ulcerative changes.

Microscopically, sarcoma of the vagina in children is usually of the round-celled and spindle-celled variety, while myxomatous degeneration occasionally occurs. In isolated cases striated muscular fibres have been observed. Sarcoma in the adult usually consists of small round cells and spindle cells; besides these, giant cells are also met with. Mucoid degeneration has occasionally been observed. Sometimes these tumours are extremely vascular, the vessel walls participating in the formation of the tumour (angio-sarcoma) (fig. 5). Finally, endothelioma has been observed in the vagina, arising from the endothelium of the lymphatic vessels.

C.—DISEASES OF THE UTERUS.

(1) **Inflammation and Infective Granulomata.**

(a) INFLAMMATION.

In considering this question, inflammatory conditions of the mucous membrane must be distinguished from those of the parenchyma. The latter are very rare, whilst the former are important, not only because they may give rise to symptoms precisely similar to those of new growths of the mucous membrane, but because the differential diagnosis under the microscope between inflammatory changes and new growths often presents considerable difficulties.

Thus, erosion resembles carcinoma, glandular endometritis resembles adenoma, and interstitial endometritis, decidual changes, or sarcoma. These difficulties make it essential that all investigations should be undertaken with especial care, and that the material to be examined, especially in doubtful cases, should be most carefully preserved and embedded. If a sufficiently large piece of tissue can be obtained, an attempt may be made to establish a rapid diagnosis by one of the methods given

above (see page 7); if the amount of material is small, it is better to embed at once in celloidin, after careful hardening, before dealing further with it.

As regards obtaining material, it is best while curetting not to be content with a single stroke, but as far as possible to remove the whole of the uterine mucous membrane. Unless this be done a circumscribed new growth may easily be missed. Similarly, in excising suspicious ulcerations of the portio or of the cervix, it is always best to remove a considerable wedge of tissue, the base of which includes as much as possible of the ulcer, and the apex of which extends deeply into the muscular tissue. Suspicious ulcerations should never be superficially removed or merely scraped, as the most important point in their examination is to determine their relationship to the deeper-lying structures.

Histologically, inflammatory changes may affect the portio, the cervix, or the body of the uterus. The peculiarity of the changes in the portio necessitates a separate description, although, strictly speaking, they belong to, and result from, endocervicitis.

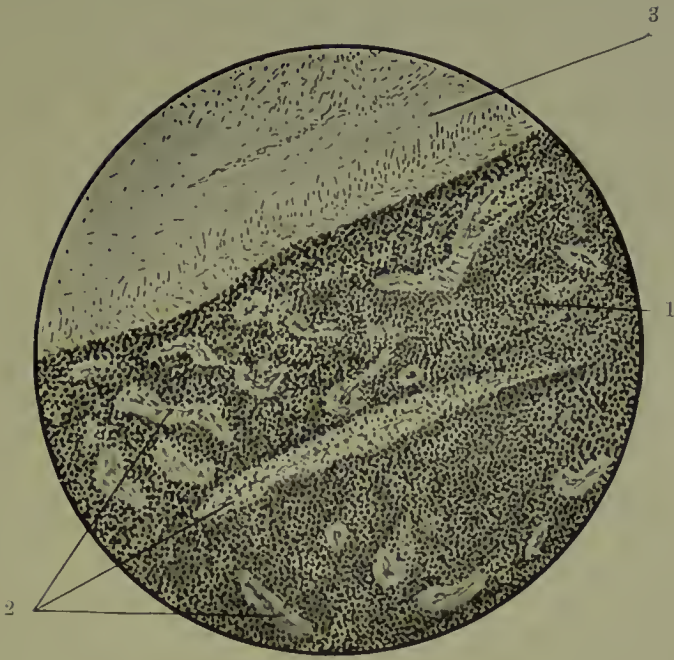
(I) EROSIONS OF THE PORTIO.—Inflammations of the portio, or so-called erosions, may be divided into true and false. In the former a real ulcerated surface devoid of epithelium exists, in the latter the ulcer is still covered with epithelium.

Four different forms of erosion are recognised: (i.) granular, a true erosion or ulcer of the portio; (ii.) simple; (iii.) papillary; (iv.) follicular. The three last varieties are really only false erosions, since with these there is no loss of the surface epithelium, but a substitution of the cervical epithelium for that of the portio. Inflammatory changes are often combined with those due to erosion.

(i.) *Granular Erosion, or Ulcer of the Portio.*—This occurs as an ulcerated surface, varying from the size of a pin's

FIG. 5.

ANGIO-SARCOMA OF THE VAGINA.

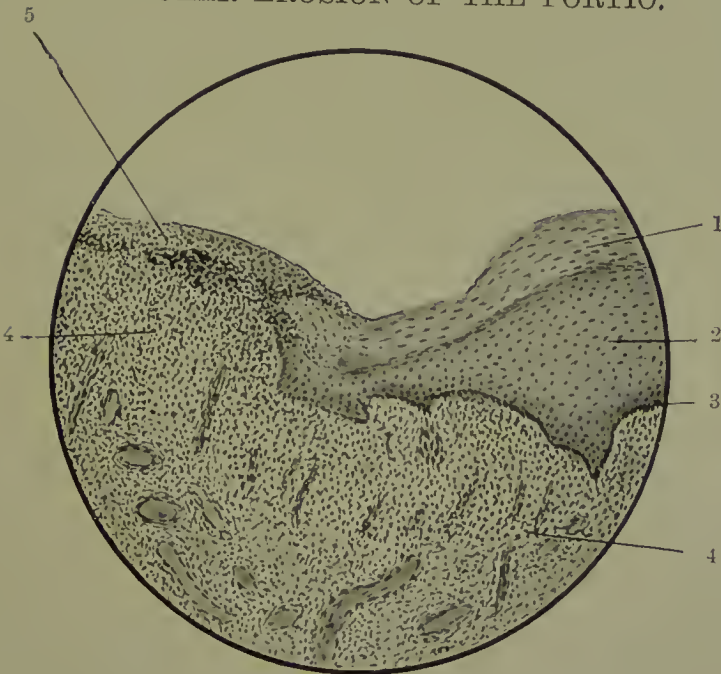


1. Small round-celled sarcoma cells.
2. Vessels with thickened adventitia.
3. Paravaginal connective tissue.

(Hæmatoxylin-eosin stain.)

FIG. 6.

GRANULAR EROSION OF THE PORTIO.



1. Stratum corneum.
2. Stratum mucosum.
3. Margin of the papillæ.
4. Small-celled infiltration in the corium, with extreme vascular injection.
5. Granulation tissue in place of superficial epithelium.

(Hæmatoxylin-eosin stain.)

head to that of a shilling. It is intensely red, bleeds easily on touch, and usually has regular sharp elevated edges. Smaller multiple ulcers of this sort are found in connection with senile colpitis. Large ulcers sometimes arise from the use of caustics, or from traumatism. They also result from the pressure of pessaries, or occur as the so-called "decubitus ulcers" in prolapse of the uterus. Finally, they are seen as a result of inflammation of the mucous membrane, the surface epithelium being destroyed.

Microscopically in this form of erosion, the superficial epithelium over the affected areas is completely wanting. Its place is taken by granulation tissue consisting of small round cells, and numerous overfilled capillary vessels. The small-celled infiltration extends along the vessels into the deeper tissues (fig. 6).

Both glands and papillæ in the vicinity of the erosion may completely disappear, the squamous epithelium in the transition region being diminished and in places lifted off from the inflamed tissues beneath.

(ii.) *Simple Erosion*. — This, together with the two following forms, is distinguished from granular erosion in its naked-eye characters, chiefly in not being limited to one or other of the lips of the portio. It usually occurs as a broad intensely red area round the os externum. A simple erosion has generally a smooth velvety surface, with sharp irregular margins. Microscopically, the tall cylindrical epithelium of the cervical mucous membrane extends over the portio and replaces the squamous epithelium. This may occur gradually and evenly, or elevated areas are seen with no attempt at transition changes. The sub-epithelial connective tissue is richly supplied with capillary vessels in the neighbourhood of which extensive areas of small-celled infiltration occur. Occasionally, in simple erosion, glands resembling those of the cervix are seen beneath the cylindrical epithelium covering the erosion.

(iii.) *Papillary erosion*.—This variety is apparently an advanced stage of simple erosion. It is characterised by numerous papillary projections which either arise from a down-growth of the cylindrical epithelium into the connective tissue, or by a papillary proliferation of the inter-glandular stroma which in the end projects above the surrounding tissues (fig. 7).

Within the papillæ numerous dilated gland-lumina occur, while intensely injected vessels and infiltrations of small cells arranged in groups or bands are frequently met with.

The cylindrical epithelium of the surface and that of the glands is tall, and contains numerous goblet cells. According to the depth of the depressions, or the height of the papillary projections, these forms of erosion often present the appearance of a deeply fissured ulcer, and thus by their naked-eye appearances may easily be mistaken for a carcinomatous new growth: microscopical examination, however, easily settles the question.

(iv.) *Follicular or Cystic Erosion*.—This is distinguished from the previous forms by the occurrence of numerous cystic cavities. These may result from single papillæ adhering to one another after loss of their epithelium and forming new cavities, or by the existing glands becoming blocked and dilated by their own secretion. The numerous, closely lying, distended cysts (Ovula Nabothi) give an uneven nodular appearance to the erosion. The cystic cavities sometimes extend beneath the neighbouring squamous epithelium of the portio, and by the pressure they exert cause it to disappear (fig. 8).

Microscopically, the cystic cavities are lined with a low cylindrical or cubical epithelium. As a result of the increasing pressure of the contents, the connective tissue septa as well as the superficial epithelium gradually become thinner, and in places may entirely disappear. The development of vessels and small-celled infiltration in their neighbourhood is usually scanty.

FIG. 7.

PAPILLARY EROSION OF THE PORTIO.

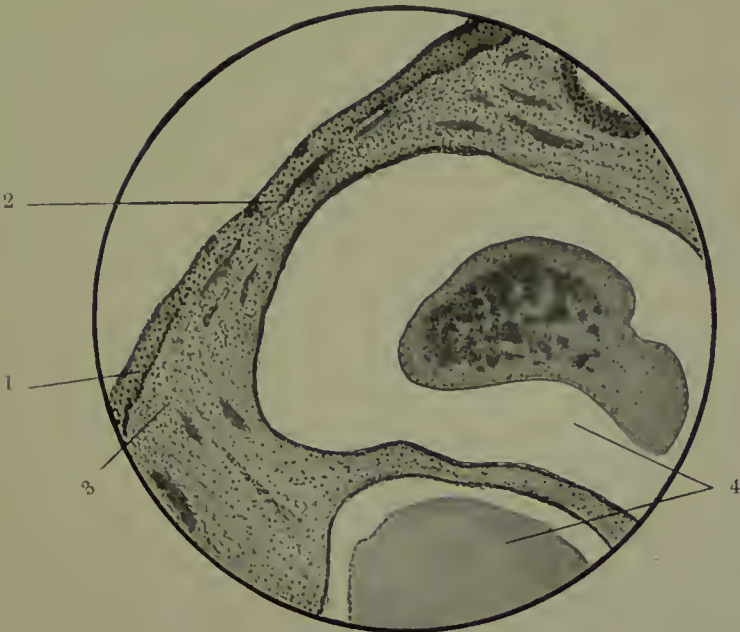


1. Exuberant papillae covered with cylindrical epithelium.
2. Small-celled infiltration within the papillae.

(Hæmatoxylin-eosin stain.)

FIG. 8.

FOLLICULAR, OR CYSTIC EROSION, OF THE PORTIO.



1. Squamous-celled layers which are diminished in height.
2. Area of granulation tissue taking the place of the surface epithelium.
3. Small-celled infiltration in the sub-epithelial connective tissue.
4. Cystic gland-cavities (follicular cysts; Ovula Nabothi), containing mucoid material and round cells.

(Hæmatoxylin-eosin stain.)

Erosions may heal completely, either by the squamous epithelium of the portio growing over or beneath the cylindrical epithelium and invading the superficially placed erosion glands, or else, the cylindrical epithelium as a result of proliferative changes is converted into squamous epithelium. Erosions may sometimes become malignant by abnormal proliferation of the epithelium: carcinomata arising in this way are termed cancerous erosions.

Erosions must not be confused with ectropion of the cervical mucous membrane. This results either from lateral tears in the cervix during parturition, or it may be congenital. Ectropion is not necessarily associated with inflammation, although it is clear that the exposed cervical mucous membrane is liable to both inflammatory and traumatic changes.

(2) ENDOCERVICITIS. — Inflammation of the cervical mucous membrane rarely occurs alone, being nearly always associated with endometritis of the body of the uterus. It is recognised macroscopically by intense swelling and redness of the mucous membrane together with an abundant secretion of tenacious mucus or muco-pus. Microscopically there is an extensive infiltration of small cells in the interglandular tissue, associated with intense vascular injection and capillary increase. The glands are increased in number (hyperplasia), producing an abundant secretion, while proliferative changes may be observed in the gland epithelium. The glands, moreover may be increased in size (hypertrophy), and converted into cysts. The exuberant growth of the mucous membrane sometimes leads to the formation of polypi.

(3) ENDOMETRITIS OF THE BODY OF THE UTERUS. — Specimens of uterine mucous membrane removed by the curette in order to establish a diagnosis may show well-marked naked-eye differences. It is important to note

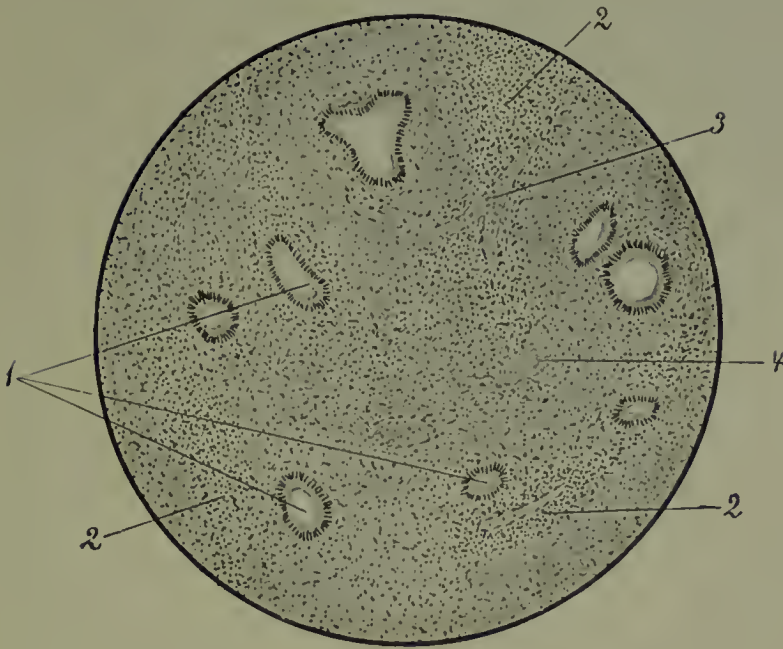
how much mucous membrane has been removed, whether the removed pieces are small and brittle, or if they appear as large coherent shreds, and whether the colour of the membrane appears pale or reddened. Where the mucous membrane has undergone fatty degeneration a well-marked yellowish colour may be seen. Similarly in a much thickened spongy mucous membrane a number of small cavities may occur, due to increase and dilatation of the glands. A friable consistency of the removed mass points to carcinoma, but a similar brittle condition of the mucous membrane may be met with in tubercle. Polypoid growths of the mucous membrane are equally easy to recognise with the naked eye; with a little practice old decidual and membranous fragments may be differentiated. From an anatomical point of view endometritis may be divided into three principal varieties according as the inflammatory changes affect the interglandular tissue, the glands, or both of these:—(i.) Interstitial endometritis; (ii.) glandular endometritis; (iii.) diffuse, or fungous, endometritis.

(i) *Interstitial Endometritis*.—In interstitial endometritis, as in most inflammations, there is an acute and a chronic stage. In the former, the mucous membrane is swollen and reddened, and in some cases œdematous. In more chronic cases, the mucous membrane may be thinner than normal, and may eventually become atrophied. Microscopically, in the acute and sub-acute stages, the interstitial tissue is infiltrated with numerous round cells. These may be arranged in groups or in the form of bands, and are distinguished from the cells of the stroma by their more intense staining capacity. The round-celled infiltration is most pronounced in the region of the capillary vessels, which are dilated and numerous, while extensive hæmorrhages may occur within the interstitial tissue (fig. 9).

At this stage, the cells of the interstitial tissue are

FIG. 9.

INTERSTITIAL ENDOMETRITIS.

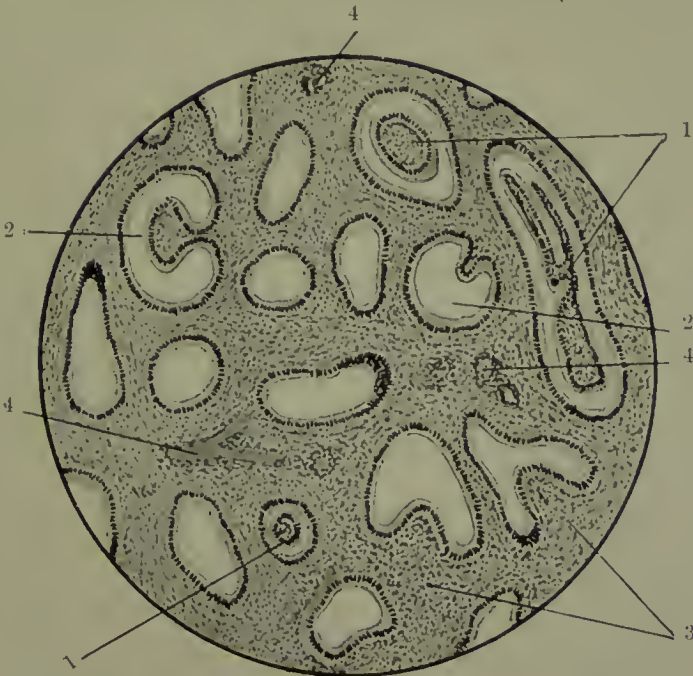


1. Atrophic uterine glands.
2. Small-celled infiltration into the interstitial tissue.
3. Injected vessels.
4. Patch of hæmorrhage.

(Hæmatoxylin-eosin stain.)

FIG. 10.

HYPERPLASTIC GLANDULAR ENDOMETRITIS (TRANSVERSE SECTION).



1. Glandular invaginations.
2. Glands showing commencing invagination of the epithelium.
3. Small-celled infiltration into the interstitial tissue.
4. Vessels in section.

(Hæmatoxylin-eosin stain.)

scarcely altered, and contain rounded deeply stained nuclei and very scanty protoplasm. As a consequence of the changes in the interstitial tissue, the glands are either pressed asunder or compressed, so that they appear smaller, less numerous, and more irregular in shape.

In chronic stages, spindle-shaped cells as well as round cells appear in the interstitial tissue and spread in long lines through it, or they may be arranged concentrically around the compressed gland lumina. By this means the interstitial tissue resembles fibrous connective tissue, especially in the atrophic stages of the disease. The vessels are decreased in number, but may be distinguished by their thickened walls and tortuous course.

The stroma cells proper also undergo certain changes. They become larger by an increase of their protoplasm, which is often very granular, while in other cases they closely resemble decidual cells. They also become more spindle-shaped, whilst their capacity for staining diminishes as compared with normal stroma cells, or those found in acute inflammation. The glands may become atrophied, while in other parts, they become cut off in consequence of the shrinking of the interstitial tissue, and by retention of their own secretion are converted into small cysts.

Two varieties of interstitial endometritis may be distinguished, namely, an *exudative* form in which portions of the connective tissue stroma become saturated with serum, and an *hæmorrhagic* form, in which numerous extravasations of blood of various sizes occur.

In differential diagnosis, care must be taken not to confuse interstitial endometritis with the decidual changes in the uterine mucous membrane, or with sarcomatous degeneration. It must be remembered that the whole mucous membrane of the uterus takes

part in the formation of the decidua, whilst in interstitial endometritis the distribution of the enlarged stroma cells is not uniform. Decidual cells, moreover, almost always resemble one another, whilst enlarged stroma cells display great variety both in size and shape. Finally, decidual cells lie closely together, and are only separated by a very thin homogeneous intercellular substance. The intercellular substance between enlarged stroma cells is much looser and more filamentous in structure.

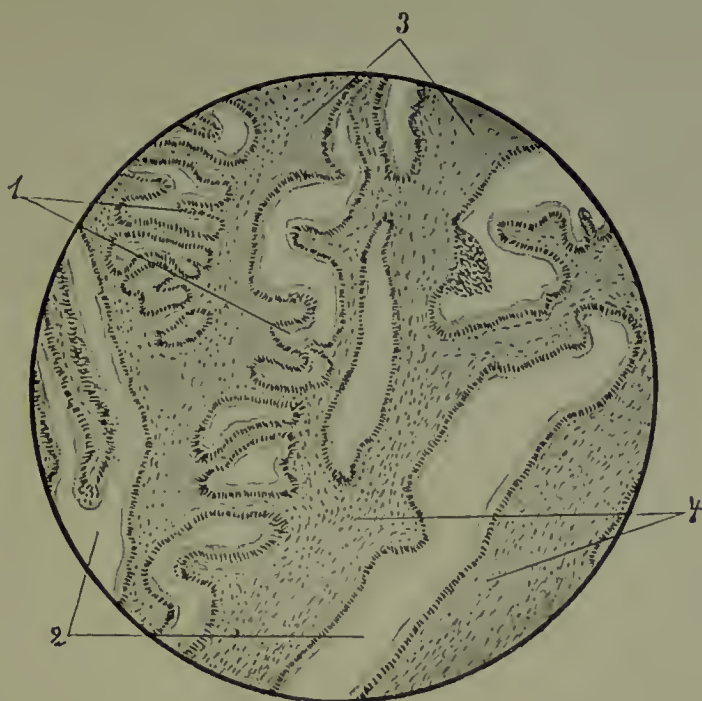
In comparing interstitial endometritis with sarcoma of the uterine mucosa, it should be remembered that in the latter an extraordinary variety in the size and shape of the cells is met with, as well as differences in their staining capacity. Besides this, in sarcoma, numerous nuclear segmentation figures are seen, and isolated necrotic or hæmorrhagic areas.

(ii.) *Glandular Endometritis*.—Two forms of glandular endometritis can be distinguished. In one case there is an increase in the *number* of the glands, and in the other an increase in their *size*. The former is termed hyperplastic glandular endometritis, and the latter hypertrophic glandular endometritis.

(a) *Hyperplastic Glandular Endometritis*.—In this variety the mucous membrane is much thickened, the changes in the epithelium and glands being the result of inflammatory irritation. Active changes affecting the epithelium lead to the formation of invaginations from the surface of the mucous membrane.

The deeper lying glands show repeated branching projections, which by gradual enlargement and constriction may develop into new glands. On making transverse or longitudinal sections through the mucous membrane an extraordinary multiplication of the number of gland lumina is at once evident, although their size is not much altered (fig. 10).

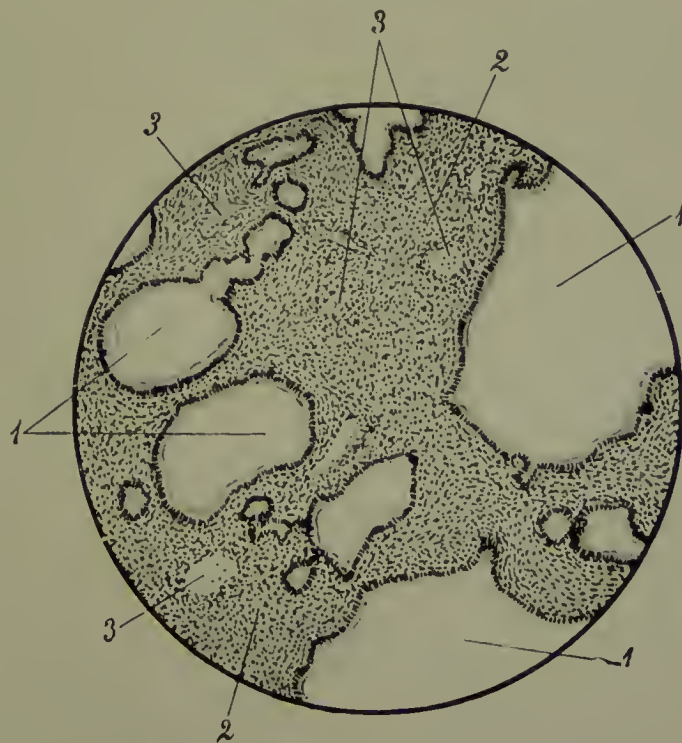
FIG. 11.
HYPERTROPHIC GLANDULAR ENDOMETRITIS (LONGITUDINAL SECTION).



1. Markedly tortuous gland lumina, the lumen repeatedly appearing in the section.
2. Hypertrophied glands, with epithelial invaginations.
3. Interstitial tissue into which exudation has taken place.
4. Small-celled infiltration into the interstitial tissue.

(Frozen section ; hæmatoxylin-picric stain.)

FIG. 12.
HYPERTROPHIC GLANDULAR ENDOMETRITIS.
(ENDOMETRITIS ECTATICA S. CYSTICA.)
TRANSVERSE SECTION.



1. Much dilated gland lumina.
2. Interstitial tissue infiltrated with small cells
3. Vessels in section.

(Hæmatoxylin-eosin stain.)

One fact must be remembered, viz., that the cylindrical epithelium always remains single-layered, even when it is impossible to trace any normal regularity in the growth of the epithelial cells. Variations are met with not only in the size but in the position of the cells, and sometimes it appears as if the cylindrical cells have been forced upwards from their basement membrane towards the gland lumina. Numerous nuclear segmentation figures indicate epithelial proliferation, which is often very active. In very acute stages of inflammation, numerous leucocytes are seen lying between the epithelial cells, and filling the gland lumina. Inflammatory changes may also affect the interstitial tissue, though not to any great degree.

Here and there areas of small-celled infiltration and exudation are seen separating the stroma cells from one another.

(β) *Hypertrophic Glandular Endometritis*.—In contrast with the previous form of inflammation, a special feature of this variety is the enlargement of the already existing glands. The proliferation of epithelial cells may either lead on to an enlargement of the glands in a longitudinal direction, or to a remarkable increase in their breadth. If the expansion of the glands in a longitudinal direction is resisted by the muscular layers or interstitial connective tissue, the glands become folded, tortuous, or curled like a corkscrew, while well-marked invaginations are met with (fig. 11).

In longitudinal or transverse sections of the gland cavities, the most diverse appearances are seen. Increase of the glands in breadth may be irregular and lead to extensive cystic formation (fig. 12).

In some cases on naked-eye examination, the uterine mucous membrane appears completely beset with small cysts. The dilated gland lumina are, as a rule, filled with mucous or blood-stained contents. Minor inflam-

matory changes occur at the same time in the interglandular tissue, such as injection of the vessels and small round-celled infiltration. The differential diagnosis between glandular endometritis and malignant adenoma (carcinoma) is of great importance, but is only one of degree.

In adenoma malignum the proliferation and multiplication of the glands is unlimited, and the epithelium forces its way in a papillary manner not only towards the lumen of the uterus, but also into the muscular tissue. Besides this, the interstitial tissue almost completely disappears, so that the epithelial tubes lie closely together, the true glandular type being no longer evident.

In adenoma malignum, as the normal glands disappear, individual gland spaces are no longer to be found, the whole field being filled with a labyrinth of fissures and spaces irregularly massed together. The individual epithelial cells appear larger, and are sometimes club-shaped. They stain intensely, but remain single layered for a long time. As soon as the epithelium begins to be many layered the condition is really one of adenocarcinoma.

Certain sources of error must be guarded against in making a diagnosis; a very important point is to decide whether the epithelium consists of one or more layers. In oblique or transverse sections through a gland lumen, or when the section passes through the orifice of a gland, it may appear at first sight as if many layers of epithelium exist, or that the gland lumen is filled with epithelial cells. This mistake is easily made in thick sections. Wherever this many-layered condition occurs, resulting from obliquity of the section, the cylindrical cells always appear regular in form and arrangement, and stand out very clearly. In the same way the cells apparently filling up the gland lumina are distinguished by their regular mosaic-like arrangement. A regular

arrangement of cells is never seen in alveoli filled with carcinoma cells which always show great variety in form and staining capacity, as well as numerous normal and abnormal nuclear segmentation figures.

(iii.) *Diffuse or Fungous Endometritis*. — Diffuse or fungous endometritis is a form of inflammation distinguished by marked thickening of the uterine mucous membrane, often leading to polypoid growths of considerable size.

Histologically, it consists of a combination of interstitial and glandular endometritis. The interstitial and glandular forms rarely occur alone, but the former is more frequently met with than the latter.

In diffuse endometritis both forms are combined, and the inflammation is often very severe. The tissues are not necessarily uniformly affected, in one place the interstitial form may predominate, in another, the glandular. Inflammation of the interstitial tissue mostly occurs in the superficial layers of the mucous membrane, that of the gland tissue in the deeper parts. In other respects, the microscopical appearances are the same as in the interstitial and glandular forms of endometritis described above.

A fourth form of endometritis must be briefly mentioned, which, though occupying a separate position, must strictly speaking, be reckoned among the interstitial forms of inflammation. This variety is described as *Exfoliative Endometritis*, or *Membranous Dysmenorrhœa*. The characteristic feature of this variety is that during menstruation a membrane is expelled from the uterus. It may be passed entire, or in separate shreds, and often represents a complete cast of the uterine cavity with clearly recognisable openings for the tubes and os internum. The outer surface of this membrane is rough and villous, whilst the inner is smooth, and often displays a large number of small punctiform openings which correspond to lumina of individual glands.

Microscopically, inflammatory changes are found in the interstitial tissue, with well marked small-celled infiltration and a peculiar alteration in the stroma cells. These are considerably increased in size, the nuclei are rounded and stain deeply, whilst the protoplasm stains less intensely.

The cells are round or oval in shape, and lie loosely in a finely fibrillated or granular stroma. They resemble true decidual cells very closely, but the latter are more regular in form and more closely packed together so that they sometimes appear flattened.

The cells are surrounded by a very thin homogeneous intercellular substance.

The glands in the cast of membranous dysmenorrhœa are much diminished in number; their epithelium and that of the surface consists of cells of a somewhat low cubical type, whilst the form of the gland cavities is irregular when seen in transverse section (fig. 13).

For details of the decidua vera, see p. 43.

Etiologically, the various forms of endometritis have been divided into those of a bacterial and a non-bacterial origin. Under the non-bacterial group are usually included the previously described varieties of endometritis; but it cannot be said that these may *not* be due to micro-organisms. Among those having a true bacterial origin, are septic endometritis (puerperal and non-puerperal) and gonorrhœal endometritis.

These forms usually occur as purulent inflammations; the micro-organisms giving rise to them being streptococci, staphylococci, and gonococci. They occur in the secretions as well as in the tissues of the mucous membrane.

(4) METRITIS.—Inflammations of the parenchyma of the uterus are divided into acute and chronic. Acute metritis includes septic (puerperal and non-puerperal) and gonorrhœal metritis. These are both of bacterial

origin, and are always accompanied by a well marked small-celled infiltration of the intermuscular connective tissue; this usually follows the course of the vessels. In its further course acute metritis may end in abscess formation, or it may become chronic.

Chronic metritis may arise from circulatory disturbances, displacements, chronic endometritis, new growths, subinvolution, and improper therapeutic measures.

Microscopically, in chronic metritis only mere traces of small-celled infiltration are found in the neighbourhood of the vessels, the chief change noted being a hyperplasia of the connective tissue in which numerous mast cells* occur. Opinions are divided as to the participation of the muscular tissue in the inflammatory changes.

PREGNANCY CHANGES.

Only the most important changes occurring in connection with pregnancy will be dealt with here. Those of special interest are the conversion of the uterine mucous membrane into the decidua, inflammation of the decidua (decidual endometritis), and investigations dealing with retained products of conception (retention of the decidua and chorion).

(1) *Uterine Decidua*.—The uterine mucous membrane is converted into the decidua in every pregnancy, whether intra- or extra-uterine. The mucosa in intra-uterine pregnancy increases in thickness in an extraordinary manner up to the third month, then, as a result of the growth of the ovum, it is gradually flattened out. The decidua in extra-uterine pregnancy may however go on growing until the termination of the pregnancy. In premature interruption of an extra-uterine gestation where death of the ovum occurs, the decidua is usually expelled

* Mast cells = coarsely granular basophile cells.

entire. This may also occur in intra-uterine pregnancy. The decidua, cast off in this way, presents a rough villous outer surface, while internally it is smooth and wrinkled. If only portions of the decidua come away, the retained fragments may give rise to hæmorrhage, necessitating their removal. Decidual shreds removed by the curette after careful hardening, exhibit the histological structure of the uterine decidua, which in doubtful cases almost settles the question whether pregnancy has occurred or not.

Under the microscope the decidua is seen to consist of two layers—(1) a superficial cellular and (2) a deeper glandular layer. If spontaneously expelled the greater part of the glandular layer remains behind, out of which the new uterine mucous membrane is regenerated. When removed instrumentally, the decidua shows both layers. These retained glandular elements, which largely help in the regeneration of the mucous membrane, may normally be seen to extend amid the muscular bundles of the uterine wall.

The cellular layer is mainly formed of characteristic decidual cells, and in the early months of pregnancy it may contain a few glands. The decidual cells arise from the stroma cells of the interstitial tissue of the mucous membrane. They usually contain a rounded nucleus surrounded by a narrow border of protoplasm.

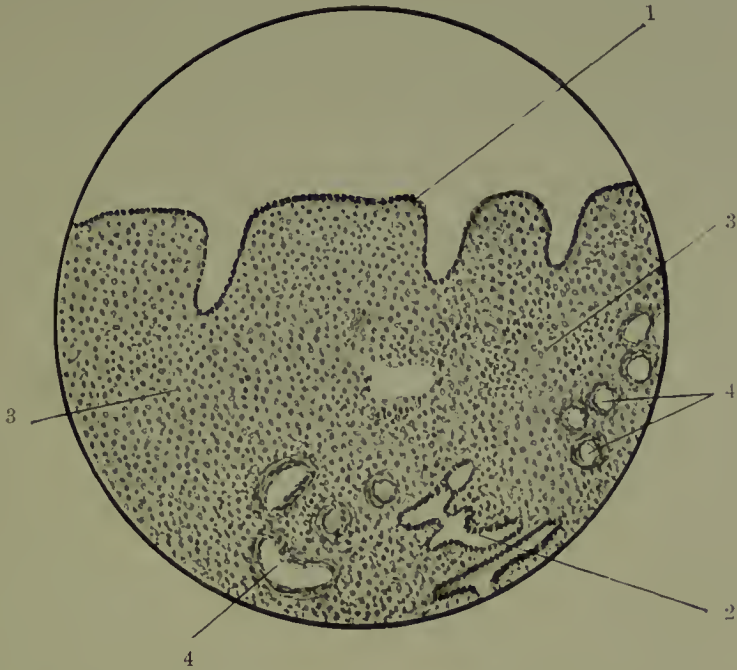
As a result of the growth of the ovum, the stroma cells of the uterine mucous membrane are greatly enlarged. The protoplasm in the first place increases, whilst the nucleus only expands to a lesser degree and at the same time becomes more vesicular in character.

Decidual cells in the early period of pregnancy (one to three months) are rounded or oval on section. As a result of lying so closely together and from the small amount of intercellular substance between them, the cells after a time become flattened, and thus often pre-

FIG. 13.

EXFOLIATIVE ENDOMETRITIS, OR MEMBRANOUS DYSMENORRHOEA.

(From a membrane which was spontaneously expelled.)

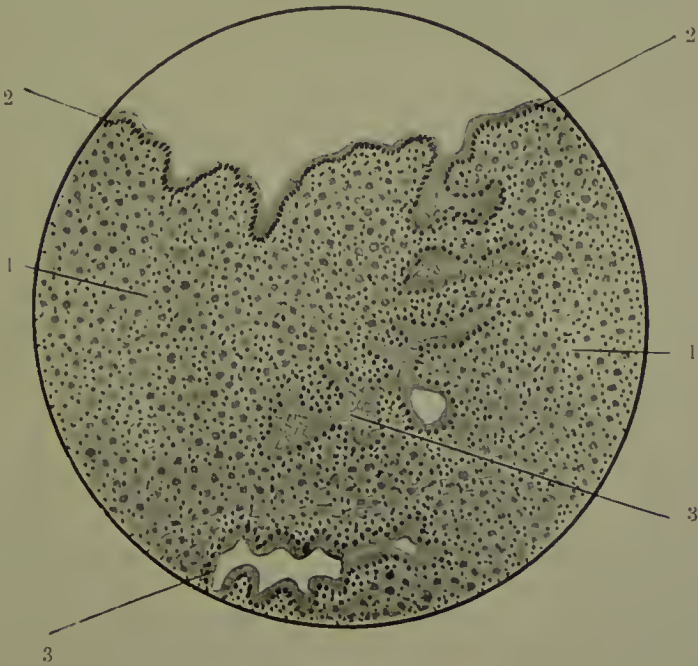


1. Flattened surface epithelium.
 2. Tortuous gland lumina.
 3. Interstitial tissue containing large stroma cells like decidual cells, and small-celled infiltration.
- (Hæmatoxylin-eosin stain.)

FIG. 14.

UTERINE DECIDUA.

(From a preparation obtained from curetting after abortion.)



1. Decidual cells.
 2. Surface epithelium.
 3. Gland lumina with swollen epithelial cells.
- (Hæmatoxylin-eosin stain.)

sent the appearance of large squamous epithelial cells. In the further course of pregnancy, the cells are much compressed by the growth of the ovum and may finally assume a spindle-shaped appearance. The intercellular tissue sometimes contains a few round- and spindle-shaped cells (fig. 14).

Distinct changes may also be observed in the glands; their number being at first diminished in the superficial layers of mucous membrane and increased in the deep layers. In the superficial layers the gland tubes are usually straight; in the deeper layers they are much convoluted, considerably dilated, and of the most varied form. Changes in the epithelium also occur; in the very earliest periods, before any proliferation of the epithelium is to be observed (which often gives rise to projections into the gland lumina) it retains its cylindrical form.

In the further course of the pregnancy the cells become flattened, expanded or cubical, and in some places are swollen and vesicular, thus closely resembling decidual cells. Towards the end of pregnancy the epithelial cells become flatter, and finally, like the surface epithelium, become endothelial in character. Sometimes a conversion of the superficial epithelium as well as of the gland epithelium into the so-called syncytium can be observed. This change consists in a gradual disappearance of the cell boundaries, so that in place of single cells, unbroken areas of protoplasm occur which stain darkly, and in which the free cell nuclei are embedded. The vessels are seen to be increased in number and distended with blood, especially in the glandular layer, their walls being usually much thinned and consisting of little more than a layer of endothelium. Here and there in their neighbourhood small collections of round cells are met with.

(2) *Decidual Endometritis*.—Inflammation of the decidua is often the cause of abortion; it may arise primarily, *i.e.*, during the pregnancy, or secondarily, *i.e.*,

it may be the continuation of a pre-existing endometritis. An inflamed decidua of this nature is often extraordinarily thickened; the thickening may affect the whole decidua or isolated parts of it, giving rise to peculiar circumscribed proliferations, which often make the decidua appear swollen and polypoid.

Microscopical examination shows that the seat of the inflammation is principally in the cellular layer of the decidua. An active small-celled infiltration occurs, separating the decidual cells, which are often increased in number. In other cases the decidual cells are lost in the inflammatory exudation. In its further course, a dense network of fibrillary connective tissue forms between the decidual cells, which become divided into groups, and often undergo fatty degeneration. In the new connective tissue thrombosed vessels and extensive hæmorrhagic areas are commonly seen.

(3) *Retention of the Decidua and Chorion.*—In the majority of cases of abortion portions of the decidua and chorion may be retained, and as these may give rise to repeated hæmorrhages they should be removed. It is often important, for diagnostic purposes, to submit the material so removed to microscopical examination.

The cause of such retention is often a decidual endometritis, which in itself may give rise to subinvolution. After childbirth, and especially after abortion, portions of the glandular layer of the decidua normally remain behind. Whilst the decidual cells, as a rule, soon perish as the result of fatty or hyaline degeneration, or from coagulation necrosis, other decidual cells become reconverted into normal stroma cells.

As a result of inflammation, a defective reconversion of the decidual cells frequently takes place. This may occur either in patches in the interstitial tissue accompanied by extensive small-celled infiltration, or else in the immediate neighbourhood of the arterioles which are often in a condition of hyaline degeneration.

Retention of portions of the chorion after abortion is not uncommon. This may lead to the formation of a so-called placental or chorionic polypus by the deposit of blood and fibrin upon and around the retained masses. In this manner, polypi with narrow pedicles are formed which fill up the uterine cavity; these sometimes extend into the cervical canal.

Microscopically, the chorionic villi are usually enveloped by blood clot or fibrin, but their appearance is very characteristic. The stroma of the villi consists of a reticular or fibrillary connective tissue containing a few spindle or stellate cells and blood vessels. The epithelial covering is formed by two layers of closely apposed cells. The inner, or so-called Langhans' cell layer, consists of large sharply defined cubical or polygonal epithelial cells, with rounded nuclei, and very transparent protoplasm. In a way, these resemble decidual cells, but the clear protoplasm of Langhans' cells as compared with the more cloudy protoplasm of decidual cells serves as a distinguishing feature; besides this, the nuclei of Langhans' cells are usually more deeply stained. The outer covering of the villi, or syncytium, consists of a deeply stained homogeneous band of protoplasm without any cell borders, in which free lying, deeply stained nuclei are embedded. The syncytium frequently gives off bud-like processes, which assume the most varied forms, and when loosened from their foundation, closely resemble giant cells (fig. 15). In the interior of this protoplasmic layer, vacuoles are not infrequently met with, whilst short cilia are sometimes seen on the surface.

As a rule, only one epithelial layer covering the villi can be recognised in the later stages of pregnancy, or when the villi have been retained for long periods in the uterine cavity after abortion. In the latter case, necrosis or hyaline degeneration sets in, so that the villi can only be recognised by their covering of fibrin, clear transparent outline, and somewhat fibrous consistency.

The origin of the syncytium has long been, and is still, a subject of dispute ; most investigators, however, now think that it is of foetal origin.

(b) INFECTIVE GRANULOMATA.

The following infective granulomata occur in the uterus : Actinomycosis, leprosy, syphilis, and tubercle. In consequence of the extreme rarity of the first two, only syphilis and tubercle will be dealt with here.

(1) *Syphilis*. — Syphilitic ulcerations occur on the portio and in the lower part of the cervical canal. They must be distinguished from non-specific ulcerations (erosions), and malignant new growths. They occur in the form of circumscribed indurated ulcers with sinuous edges and necrotic excavated bases. They are usually found on the anterior lip of the cervix. Papillary forms with raised borders likewise are met with.

Microscopically, it is difficult to distinguish them from other non-specific ulcerations, as they consist mainly of simple granulation tissue. Syphilitic manifestations in other parts are rarely wanting, and should generally suffice to establish a diagnosis.

(2) *Tuberculosis*.—Tuberculosis of the uterus occurs in the form of ulcers on the portio, tuberculous endometritis, and multiple abscesses in the uterine wall. Tuberculous ulceration of the portio is very rare, and is usually secondary ; besides this variety, cauliflower-like growths have also been observed on the portio, which were of a tuberculous nature. A tuberculous ulcer of the portio usually displays ragged undermined edges, and a yellowish base, which in places is studded with miliary nodules.

Under the microscope their tuberculous character is easily determined ; numerous characteristic nodules with epithelioid and giant cells occur, which are clearly outlined from the surrounding granulation tissue by their small staining capacity. These tuberculous nodules,

FIG. 15.

RETENTION OF THE CHORION AFTER ABORTION.

(From a specimen obtained by curetting.)



1. Reticular connective tissue stroma of the chorionic villi.
2. Syncytium, covering the outer surface of the villi.

3. Langhans' cell layer, the inner epithelial covering of the villi.
4. Bid-like processes of the syncytium.
5. Uterine glands.
6. Muscular tissue of the uterus.

(Hæmatoxylin-eosin stain.)

FIG. 16.

TUBERCULOUS ENDOMETRITIS.

(From a specimen obtained by curetting.)



1. Surface epithelium of the uterine mucosa.
2. Hypertrophied uterine glands, showing proliferation of epithelium.

3. Small-celled infiltration of the interstitial tissue.
4. Tubercle nodules with giant cells.
5. Lumen of vessel

(Hæmatoxylin-eosin stain.)

covered in some places by normal, in others by proliferated squamous epithelium, may extend into the deeper tissues. Tubercle bacilli are usually difficult to demonstrate.

Tuberculous endometritis is not very uncommon, and is often associated with tuberculosis of the Fallopian tubes. For this reason it is often possible to make a safe inference as to the nature of the disease affecting the adnexa in such cases, from the condition of the uterine mucosa. Two different forms of tuberculous disease of the mucous membrane may be distinguished—a circumscribed miliary variety, and a diffuse caseous ulcerative form:—most probably the latter condition results from the former, which may, however, exist for a long period before it breaks down. In the early stages of the disease the mucous membrane is thickened and reddened, and in some parts may be of a yellowish colour. Shreds of mucosa removed by the curette are peculiarly friable, suggesting malignant degeneration. In more advanced stages, the mucous membrane is converted into a purulent, caseous, or necrotic surface.

In the early stages of tuberculous disease characteristic microscopical appearances are found. The number of glands is diminished, the interstitial tissue is usually intensely infiltrated, and here and there, rounded areas of tissue are embedded in it, which are easily distinguished by their small staining capacity. On closer examination there is little difficulty in recognising pronounced tubercle nodules containing epithelioid and giant cells. Caseous changes can frequently be seen in the centre of these nodules, whilst in their neighbourhood an intense small round-celled infiltration is usually present (fig. 16).

In some cases tubercle bacilli may be demonstrated within the giant cells without much difficulty. Certain characteristic changes in the epithelium of the glands are of great interest. The surface epithelium may remain

normal for a long period, but the glands as a whole become diminished in number. The glands situated in the neighbourhood of the tubercle nodules are often somewhat hypertrophied and show distinct epithelial changes. The cells proliferate, and in places grow into the gland lumina in the form of papillæ. As the result of proliferation, the cells become broader and more cubical in shape, and in consequence of the increase of their protoplasm they often have a vesicular appearance—changes not unlike those already described as occurring during pregnancy.

In the further course of the disease, the nodules coalesce, caseation increases, the tissues perish more and more, so that the whole mucosa of the uterus becomes converted into an ulcerated surface. The tuberculous infection at length penetrates deeply into the uterine wall, and may lead to the formation of small multiple abscesses, pyometra, and progressive destruction. Mucous polypi existing in the uterus may also be affected by tuberculous disease, but an extension of the process to the cervical mucous membrane is extremely rare.

(2) New Growths.

(a) BENIGN NEW GROWTHS.

(1) *CONDYLOMATA ACUMINATA* (WARTS).—Warts are usually associated with a similar condition of the vulva and vagina. They may cover the whole portio up to the os externum. Their histological structure is identical with warts occurring on the vulva (p. 23).

(2) *MUCOUS POLYPI*.—Two forms of mucous polypi of the uterus can be distinguished according to their origin from the mucous membrane of the cervix or from that of the body. *Cervical* polypi grow from the region of the external os, or from the higher portion of the cervical canal, which may become dilated. Their size

varies from that of a pea to that of a hen's egg. They usually have a slender pedicle. Their surface may be smooth, and they are similar in colour to the mucous membrane of the portio and vagina. Sometimes they are uneven, nodular, or lobulated, and of an intensely red colour.

Macroscopically, these polypi are often covered with small cysts, which either contain a thin serous or a tenacious mucoid fluid. The polypi are sometimes channelled by these cysts in all directions. Their microscopical appearance varies. The superficial epithelium may be either squamous or cylindrical.

Those polypi which spring from the neighbourhood of the external os uteri are usually covered with the squamous epithelium of the portio, while those arising from the higher part of the cervical canal are covered by cylindrical epithelium, which however in long standing cases may be converted into squamous epithelium (fig. 17). This change is due to cell metaplasia.

The superficial cells, especially those of the newly converted squamous epithelium, often penetrate deeply into the interstitial tissue or into the neighbouring gland lumina, and the condition is liable to be mistaken for carcinomatous degeneration.

In other respects the structure of mucous polypi corresponds exactly to that of ordinary inflamed cervical mucous membrane, the change being most pronounced in the glands. In many cases the whole polypus is beset with numerous rounded convoluted gland lumina (ectasia). The epithelium of the glands is either of a high cylindrical form, similar to that of normal cervical glands, or else it is somewhat flattened and cubical, especially in the dilated gland cavities. The cavities usually contain mucoid material, epithelial cells, leucocytes and red blood corpuscles.

The stroma of the polypi is richly supplied with vessels,

which are often engorged with blood, while in their neighbourhood a small-celled infiltration is frequently met with. The groundwork of the stroma consists chiefly of dense fibrous connective tissue, which is sometimes in excess of the gland tissue, so that a fibrous polypus results, as opposed to the cystic or adenomatous polypus described above.

Mucous polypi of the *body* of the uterus consist of circumscribed hypertrophied portions of the mucous membrane. They may have a broad base or in other cases only a narrow pedicle. They usually grow from the fundus, especially near the orifices of the Fallopian tubes. Their colour corresponds with that of the rest of the mucous membrane. They vary greatly in size. Their histological structure differs but little from that of the various forms of endometritis, except that the individual inflammatory changes are less marked. Their surface is covered with the normal cylindrical epithelium of the uterine mucous membrane, which, however, in the larger polypi becomes flattened owing to pressure over the most exposed parts. In the majority of cases numerous distended or tortuous gland lumina occur in the interior of the polypi, which can often be made out with the naked eye. These, as a rule, contain a clear serous fluid, together with cast off epithelial cells, leucocytes and red blood corpuscles. The epithelial cells correspond with those of the uterine glands. In the distended glands, the cells appear somewhat flattened owing to the increased pressure of their contents. The stroma consists of loose fibrous connective tissue, rich in cells, with a variable number of blood-vessels. In their neighbourhood small extravasations of blood and areas of small-celled infiltration are to be observed. If the polypus projects through the cervical canal into the vagina a metaplasia may take place of the superficial cylindrical epithelial cells into squamous cells.

Tuberculous and carcinomatous degeneration of mucous polypi occurs in rare cases.

(3) CONNECTIVE TISSUE NEW GROWTHS.—Myomata are by far the most important of the innocent connective tissue new growths. Pure myomata, *i.e.*, tumours consisting entirely of unstriped muscular fibres, are rare. In most cases fibrous connective tissue is also present, so that they are more correctly described as fibro-myomata. Tumours consisting purely of connective tissue (fibromata), are also very uncommon.

(i.) *Myomata and Fibro-myomata*.—The great majority of myomata take their origin from the *body* of the uterus, *cervical* myomata being comparatively rare. The latter sometimes grow to a considerable size, and may fill up the whole pelvis. They develop either in the anterior or posterior wall, expanding the corresponding lip of the cervix, whilst the other lip surrounds the tumour like a thin capsule, the cervical canal being much distorted. In other cases, their position is retro- or para-cervical, the portio retaining its normal shape.

Myomata of the *body* are usually divided, according to their position in the wall of the uterus, into three different varieties: *submucous*, *intraparietal*, and *subserous*.

Submucous myomata usually arise from the fundus and have a broad base, or they may be pedunculated. They are rounded or oval in shape, of medium size, and are usually soft. They are nearly always covered with uterine mucous membrane, which is hypertrophied in some parts and atrophied in others.

Intraparietal myomata are surrounded by a layer of uterine tissue of variable thickness forming a capsule; they are generally spherical in form, and may reach an enormous size. They are usually hard, and are frequently multiple.

Subserous myomata arise from the peritoneal surface of the uterus, and have a pedicle of varying thickness,

which sometimes becomes twisted or completely constricted. Subserous myomata are as a rule rounded and often very hard. If they spring from the lateral wall of the uterus they may grow between the layers of the broad ligament.

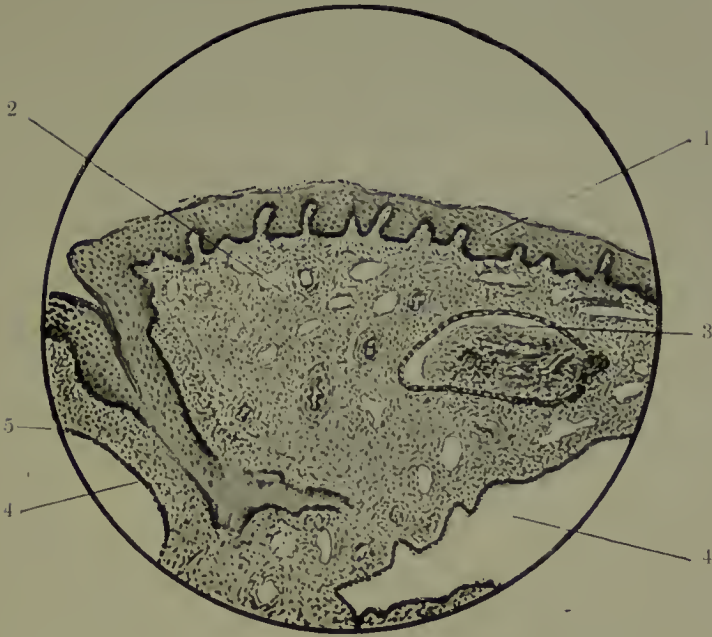
Microscopically, myomata consist of interlacing bundles of unstriped muscular fibres, and on section these are seen running longitudinally, transversely, and obliquely, in all directions (fig. 18).

In the harder varieties of myomata the number of vessels is small, whilst in the softer forms they are more numerous. The amount of intermuscular connective tissue in myomatous tumours varies to a considerable extent. In the larger tumours small bands of fibrous connective tissue with few nuclei are found. Such tumours being more correctly described as fibro-myomata. By using van Gieson's stain the muscular fibres may be differentiated from the connective tissue bundles, the fibrous tissue being stained red and the muscular fibres orange. (*Vide* p. 17.) The majority of myomata arise directly from the unstriped muscular tissue of the uterine wall; others probably arise from the muscular tissue of the blood-vessels.

Histologically, the numerous secondary changes which may affect myomata are of great interest. Widespread changes often occur in the blood-vessels and lymph vessels which undergo extensive dilatation throughout the tumour substance, causing it to assume a cystic appearance. These cavities are oblong or round in shape, and are filled with fluid blood or pale serum. Their walls are as a rule lined by endothelium. Such tumours are termed cavernous or lymphangiectatic fibro-myomata. As a result of circulatory disturbances (twisting of pedicle, thrombosis, &c.) œdematous infiltration of the myoma sometimes results, which may be either circumscribed or diffuse. This leads to the

FIG. 17.

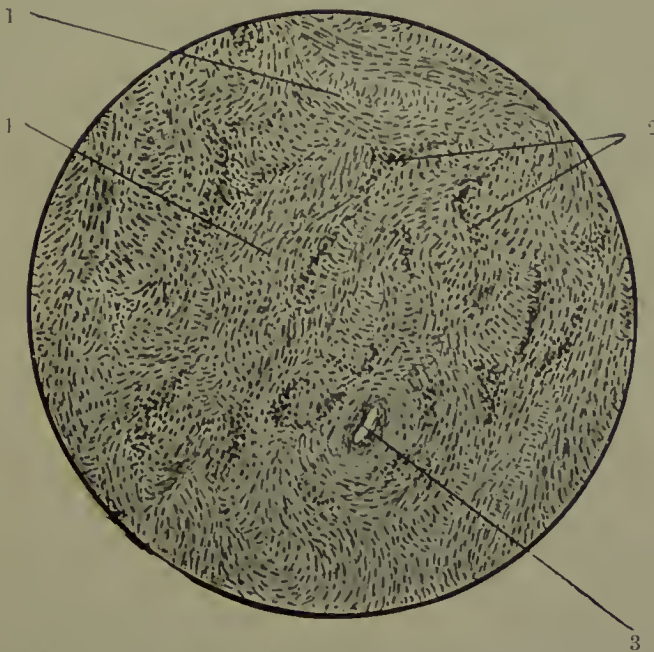
MUCOUS POLYPUS OF THE CERVIX.



- 1. Superficial squamous epithelium.
 - 2. Vascular connective-tissue stroma.
 - 3. Cervical glands, rich in cell contents.
 - 4. Dilated gland lumina, lined with low cubical epithelium.
 - 5. Deep invagination of the surface epithelium.
- (Hematoxylin-eosin stain.)

FIG. 18.

UTERINE MYOMA.



- 1. Unstriped muscular fibres in longitudinal section.
- 2. Transverse sections of muscular fibres.
- 3. Lumen of blood-vessel.

(Van Gieson's stain.)

formation of irregularly shaped cystic cavities, which however do not possess an endothelial lining.

Other retrograde changes found are fatty, hyaline, myxomatous, and more rarely, amyloid degeneration; occasionally suppuration, necrosis and calcification occur. Mixed tumours of the most varied kind are sometimes seen, for example, combinations of myoma with enchondroma, lipoma, and carcinoma. Sarcomatous degeneration is not infrequent.

(ii.) *Adeno-myoma*.—A special form of myoma must be mentioned, namely, adeno-myoma, which is characterised by the presence of gland-like epithelial tubes in its interior. Adeno-myomata arise either from the uterine mucous membrane or from the Wolffian bodies, and according to their origin, may occur in any portion of the uterine wall, but are most frequent in the posterior wall, or else near the orifices of the Fallopian tubes. In the latter case, the tumour is not as a rule sharply outlined from the surrounding structures. According to the predominance of muscular tissue or of adenomatous tissue, adeno-myomata present a hard or a soft consistency. The gland tubes lined with cylindrical epithelium, are surrounded by cytogenous connective tissue as in the normal uterine mucous membrane, and they are, moreover, systematically arranged, so that a main canal can be distinguished into which other tubes in the neighbourhood open.

(b) MALIGNANT NEW GROWTHS.

(1) *ADENOMA MALIGNUM*.—Adenoma malignum is of very rare occurrence in the cervix; it is much more common in the body of the uterus. It is very difficult, especially in their initial stages, to draw a distinction between simple hyperplasia of the glands, as is seen in endometritis, and malignant glandular neoplasms.

Any doubt however as to malignancy, is dispelled

by finding that the interglandular connective tissue in adenoma malignum becomes infiltrated with cells, and that the glandular elements encroach extensively on the muscular tissue.

An actual tumour formation however does not take place, the affected tissue macroscopically hardly exhibiting any deviation from the normal or at most it is only of a softer consistency, whilst the muscular layers in places often appear somewhat porous.

Microscopically, malignant adenoma of the *cervix*, at all events in advanced cases, has the appearance of an irregular tangle of gland lumina and long branching ducts infiltrating the whole cervix; these are all lined with the single-layered cylindrical epithelium characteristic of the cervical mucous membrane. The interglandular connective tissue remains comparatively unaltered for a considerable time. It is also unusual to find any cyst-like dilatation of the gland lumina.

Adenoma malignum affecting the *body* of the uterus is distinguished on macroscopic examination by a more or less definite thickening of the mucous membrane, which in rare cases may assume a polypoid form.

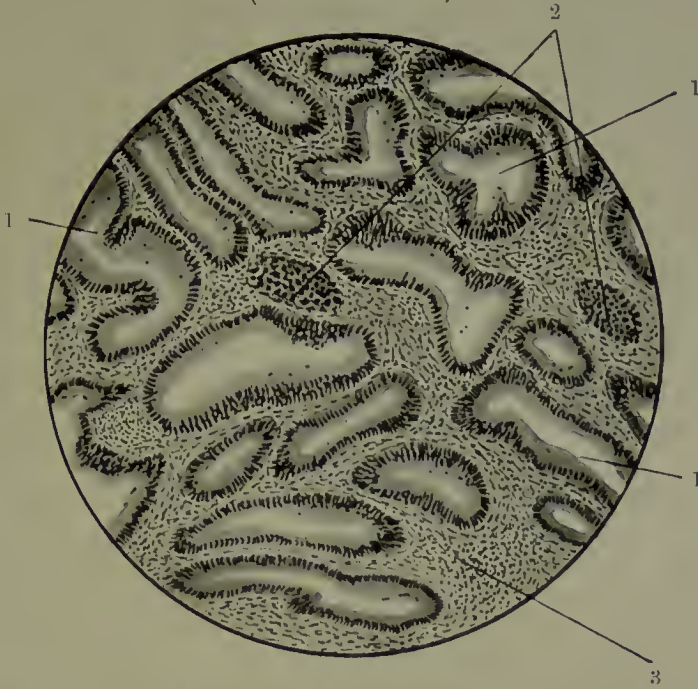
On microscopical examination of such adenomatous tissue removed by the curette, the first thing noticeable is the large amount of tissue removed, and secondly, the fact that if the muscular tissue is already involved, portions of this layer are removed at the same time. In sections, it will be noted that gland ducts and gland lumina lie irregularly side by side, so that on examination the sections, even to the naked eye, appear like a sieve (fig. 19).

The enormous increase of the glands occurs simultaneously with a corresponding decrease or crowding out of the interstitial connective tissue. This at last almost completely disappears, so that only a layer of fusiform cells is left between the gland lumina, representing the remains of the interglandular tissue (fig. 20),

FIG. 19.

ADENOMA MALIGNUM OF THE BODY OF THE UTERUS.

(EARLY STAGE.)

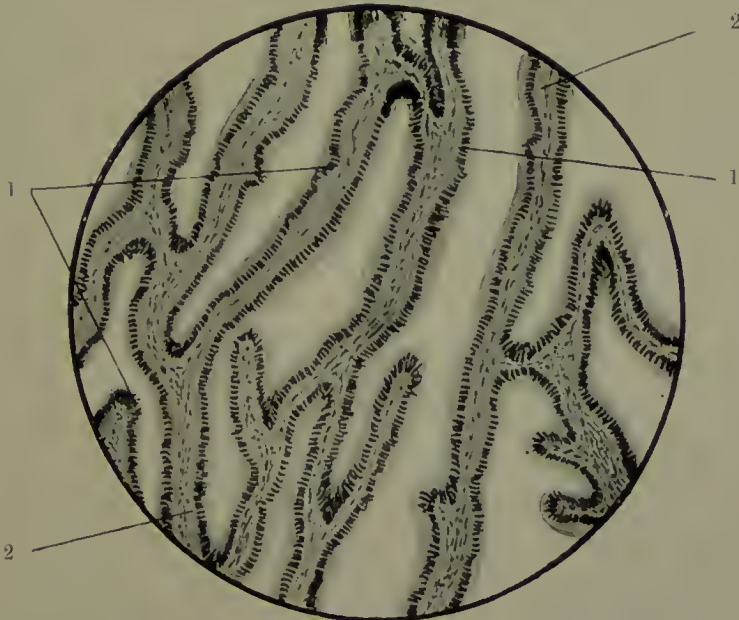


1. Longitudinal and transverse sections of gland lumina, showing papillary elevations of the epithelium.
2. Oblique sections of glands which appear to be lined with many layers of epithelium.
3. Inter-glandular connective tissue, showing small-celled infiltration.

(Hæmatoxylin eosin stain.)

FIG. 20.

ADENOMA MALIGNUM OF THE MUCOSA OF THE BODY
OF THE UTERUS.



1. Ramifying ducts, lined with well marked cylindrical epithelium.
2. Scanty interstitial connective tissue.

(Hæmatoxylin-eosin stain.)

One characteristic of these glandular growths is that although they grow closely under the surface of the mucous membrane, they frequently penetrate deeply into and infiltrate the muscular tissue. In the latter case, however, the fact must not be forgotten that the existence of isolated but regularly formed glands amid the muscular tissue is, under normal conditions, not of very great rarity.

More minute histological examination of adenoma malignum shows that two different varieties may be recognised. The increase in the glandular elements arises either by the epithelium forming papillary masses which grow inwards towards the lumen of the gland, or by the epithelium growing outwards in a tubular manner into the tissues. In the former case it may be termed "inverted," in the latter "everted" (fig. 21). In both cases, constriction or sequestration of the inverted or everted epithelial tubes may occur, leading to a new growth consisting of glandular tissue.

The glandular epithelium exhibits various deviations from the normal. Numerous nuclear segmentation figures occur, in which the axes of segmentation always run parallel to the cell base. Moreover, the cells are increased in height, and are much more thickened and club-like than those of the normal epithelium.

As long as the adenomatous character of the growth persists, the epithelium consists of a single layer. The transformation into carcinoma is signalled by the appearance of several cell layers, while the axes of the segmentation of the nuclei are now arranged vertically to the cell base. This is characteristic of carcinoma.

Scattered amid the interglandular connective tissue, centres of small round-celled infiltration may be seen. The blood-vessels are few in number, being crowded out by the proliferation of the glandular elements.

It is exceedingly difficult even for experienced in-

investigators to decide whether pieces of mucous membrane removed by the curette are innocent (endometritis glandularis), or whether they have already undergone malignant changes (adenoma malignum). This may be seen by comparing figs. 19, 20, and 21, which are all taken from the same uterus.

Appearances such as are seen in fig. 19, are typical of simple glandular endometritis. In fig. 20 the epithelial tubes are more suspicious, the loss of the actual glandular type and the gradual atrophy of the stroma being distinctly perceptible. In fig. 21 no doubt as to the malignancy of the new growth can be raised, as the epithelial tubes have already penetrated the muscular layers in all directions and in great numbers.

(2) CARCINOMA OF THE UTERUS.—Cancer of the uterus occurs in three principal forms depending on the situation of the growth, viz., cancer of the portio, cancer of the cervix proper, and cancer of the body. These forms may occur separately, or in conjunction with one another; a combination of cancer of the portio and cancer of the cervix being most frequently found.

(i.) *Cancer of the Portio*.—Cancer of the vaginal portion of the cervix appears macroscopically in two principal forms; either as a *polypoid carcinoma*, also termed a cauliflower excrescence, or as an *infiltrating cancer*—the actual carcinomatous ulcer.

The *polypoid* variety is usually circumscribed, and arises from either the anterior or posterior lip, or in rare cases even from both. It has either a broad base or may sometimes have a thick pedicle. The size varies from that of a cob-nut to a fist; in some cases the growth may fill the whole vagina, concealing the healthy part of the portio and the os externum. The surface of a cauliflower excrescence may remain quite smooth for a long time, so that the tumour resembles a benign polypus of the mucous membrane. In other

cases its surface is lobed, and covered with small papillary excrescences. In the later stages ulceration takes place on the surface which becomes covered with a yellowish-grey slough.

The *infiltrating* variety of cancer is distinguished from the previously described form by its tendency to involve the whole vaginal portion. In advanced cases it may also attack the mucous membrane of the cervix and vagina. At first the carcinoma involves the "niveau" of the mucous membrane of the portio, and possesses raised tumid borders. Its centre presents extensive disintegration and crater-like cavities, which eventually involve and destroy the deeper tissues.

It is characteristic of this form of disease that the growth is always very friable, and notwithstanding a certain firmness of the main mass of the tumour it is easy to break away portions of the growth with the finger nail. The patient often observes a great tendency to hæmorrhage (bleeding on coitus being frequently noticed as the first symptom).

From a histological standpoint, two forms of carcinoma of the portio can be differentiated, viz., a squamous-celled carcinoma and a cylindrical-celled carcinoma.

(a) *The Squamous-celled Carcinoma or Cancroid*.—This originates in the superficial epithelium of the portio, and as a rule exhibits the typical aspect of horny cancer (Hornkrebs). The epithelial depressions between the papillæ grow downwards and proliferate in an irregular manner. Solid processes of epithelial cells and cones of different sizes are formed, which infiltrate and displace the subcutaneous tissues in all directions. All the normal connective tissue constituents, such as glands, vessels, &c., are replaced during the further course of the disease by the unlimited proliferating new growth. Finally only a few thin connective tissue septa are left, which separate the epithelial centres from one another, thus

causing the new growth to assume almost an alveolar character (fig. 22). Within the interstitial stroma of the growth, in its early stages, numerous vessels and extensive areas of small-celled infiltration are found. This occurs chiefly at the edge of the growth, and may be put down to a reaction of the healthy tissues to the cancerous invasion.

The small-celled infiltration in the tissues is easily distinguished in stained preparations by its deeper colour, which shows up against the paler areas of cancer cells which it encloses. In unstained sections, extensive areas of fatty degeneration are frequently seen in the stroma, and in consequence of their deeper shade stand out conspicuously against the pale cancer nests.

The superficial epithelium mostly remains intact during the early stages of the growth, but various changes are sometimes observed in the cells; for example, the prickle and ridge cells of the stratum mucosum are apt to disappear early while the superficial stratum of epithelium gradually becomes more and more flattened. In some places broad vascular papillæ which are infiltrated with round cells appear on the surface, and become transformed into granulation tissue; this is sharply bordered off by a deep furrow from the normal squamous epithelium.

The cancer cells themselves are distinguished by their manifold shape and size, and though at first the regular type of squamous epithelial cells is maintained, all regularity is soon lost, or is only found in the marginal cells of the cancerous cones and nests. These frequently assume a more or less cylindrical type, and are remarkable on account of their power of absorbing staining reagents. Towards the centre of these cones and processes the staining is less deeply marked, possibly on account of their poorer nutrition. Characteristic concentrically layered cancrioid pearls are not uncommon.

FIG. 21.

ADENOMA MALIGNUM, INVOLVING THE MUSCULAR TISSUE OF THE
BODY OF THE UTERUS.

"Everted" form; from the same preparation as figs. 19 and 20.

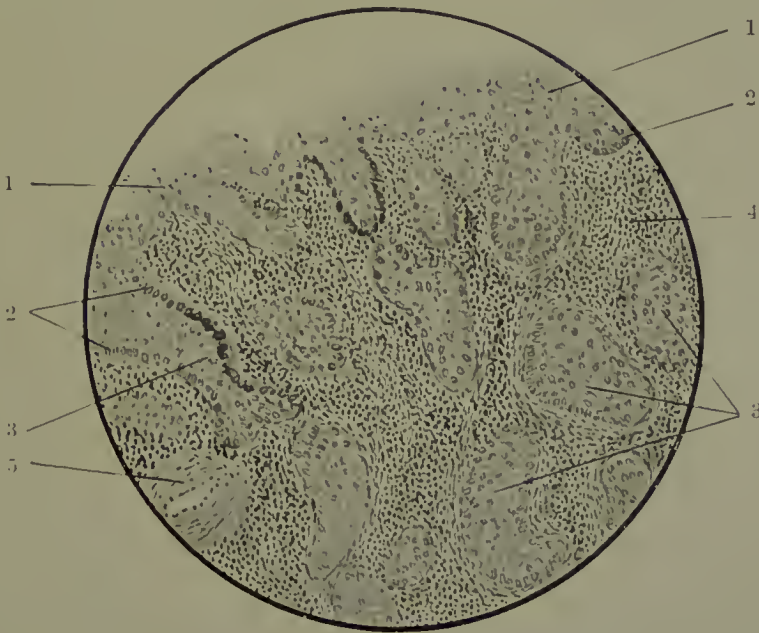


1. Glandular elements penetrating from the mucosa into the muscular layers.
2. Adenomatous tissue within the muscular layers.
3. Transverse section of muscular bundles.
4. Longitudinal section of muscular bundles.

(Hæmatoxylin-eosin stain.)

FIG. 22.

SQUAMOUS-CELLED CARCINOMA OF THE PORTIO.



1. Superficial epithelium with cone-like processes of cells penetrating into the deeper tissues.
2. Epithelial cells which are still regularly arranged, those at the edges being more deeply stained.
3. Cancer-cells arranged in a cone or nest-like form.
4. Connective tissue showing small-celled infiltration.
5. Vessel in transverse section.

(Hæmatoxylin-eosin stain.)

Sometimes areas of degeneration, eventually leading to necrosis, occur in the same situation. Asymmetrical nuclear segmentation figures (giant mitoses, multipolar mitoses) frequently occur which are particularly characteristic of cancer cells, as well as various processes of degeneration (hyaline, myxomatous, fatty, calcareous, &c.)

(β) *Cylindrical-celled Carcinoma*.—This may originate either from the surface of an erosion covered with cylindrical epithelium, or in rarer cases from the deeply placed erosion glands. In the former case, the superficial epithelium is at first more stratified, while the original tall cylindrical epithelium becomes of a lower type, assuming a cubical and finally a polymorphous form. It is noteworthy that in atypical proliferation of the epithelium, the axes of the segmentation of the nuclei do not (as in innocent growths) run parallel to the cell base, but are placed perpendicularly. The newly formed cells no longer lie next to one another, but are superimposed, thus giving rise to many strata of cells. During the further course of the growth, this many-layered epithelium penetrates as conical processes into the underlying tissues, forming irregular epithelial tubes and nests which crowd in upon the sub-epithelial structures. The glands are either compressed or the cancer cells push forward the epithelial lining; eventually they break through into the gland lumen and there proliferate indefinitely. During these processes, the gland epithelium however sometimes remains unaltered.

In the second variety, where the cancer starts from erosion glands, the conditions are different. In this case, the first changes noted are that the tall cylindrical epithelium lining the glands tends to change its shape and to become many-layered. The gland lumina are crowded with proliferated cells, or there remains in the centre only a small lumen as a relic of the original

gland. However, the fact must not be overlooked that similar centres may occur secondarily in the solid epithelial cones and nests, due to degenerative changes in the cells. The atypical proliferation of cells does not however confine itself to gland lumina, but conical protrusions and processes are formed which penetrate irregularly into the interglandular stroma. According to the amount of stroma existing, the tumour may be hard or soft in consistency.

Should the glandular type be maintained for a considerable time, the neoplasm is termed an adeno-carcinoma, the cancer cells preserving their tall cylindrical type, while their longitudinal axes are directed perpendicularly to the alveolar margins. The processes of degeneration mentioned above also occur in cylindrical-celled cancer of the portio.

(ii.) *Carcinoma of the Cervix*.—In carcinoma of the cervix proper, two forms are to be differentiated—a *superficial infiltrating* carcinoma of the mucous membrane, and *carcinomatous nodules* occurring in the walls of the cervix; the latter is a true glandular carcinoma.

The superficial variety originates in the mucous membrane of the cervical canal which is soon completely involved by the new growth. From this the carcinoma quickly penetrates into the more deeply situated portions of the cervix. Deep crater-like cavities result owing to superficial sloughing of the growth. Coincident with the advance of the disease into the cervix there is also a general thickening, so that the size of the cervix may exceed that of the body of the uterus. On superficial examination this condition might be mistaken for a myoma of the cervix. Should the changes be accompanied by early ulceration and destruction, a correspondingly large cavity with rigid walls results.

The second form of cancer of the cervix in its early stages, occurs as firm isolated nodules amid the tissues

of the cervical wall. The nodules stand out from their surroundings, and are distinguished by their lighter colour. Such nodules may be covered by the perfectly normal mucous membrane of the cervical canal, and even by a thin stratum of muscular tissue. As the disease progresses it breaks through into the cervical canal, as well as on to the surface of the portio vaginalis.

On microscopical examination, carcinomata of the cervix proper are cylindrical-celled cancers, their origin being either from the superficial epithelium of the canal, or the more deeply seated cervical glands. The development of such growths is similar to cylindrical epithelial cancer arising in the portio. The superficial epithelium becomes many layered and polymorphous, and penetrates in conical masses into the deeper tissues, where it forms broad epithelial tubes and nests (fig. 23). These are surrounded by a stroma, which is infiltrated with small cells.

When the carcinoma originates from the cervical glands, a multi-stratification of the cylindrical cells soon takes place gradually leading to an occlusion of the gland lumina, while cone-like processes of epithelial cells are seen projecting into the surrounding tissues. The consistency of the tumour is generally soft and marrow-like, and is due to a preponderance of the cancer alveoli over the stroma, which is often very deficient.

Squamous-celled carcinoma of the cervix may arise in two ways: in the first, the squamous epithelium of the portio may extend into the cervical canal as in the process of healing of an erosion, and there may undergo an atypical epithelial proliferation; in the second, the original cylindrical epithelium becomes changed by metaplasia into squamous epithelium and then undergoes further proliferative changes. A corresponding metaplasia and proliferation of the surface epithelium may occur not only in the cervix, but also in the body of the uterus and the Fallopian tubes. (*Vide* fig. 38.)

Histologically, in other respects squamous-celled carcinoma of the cervix closely resembles that occurring in the portio.

Another variety of cancer which occurs with particular frequency in the cervix is *carcinoma lymphaticum*. It apparently arises from glands which lie deeply in the muscular tissue of the cervix. This form of disease spreads principally, if not exclusively, by means of the lymph channels.

Microscopically, this variety is peculiar in that instead of finding broad epithelial cones and rounded nests of cells, long narrow epithelial areas with dendritic ramifications occur. These communicate with one another, and follow the course of the lymphatic vessels (fig. 24). This form of cancer may occur independently, but at other times it is seen in conjunction with other forms, such as those already described.

(iii.) *Carcinoma of the Body of the Uterus*.—Macroscopically, two chief varieties of cancer of the body can be distinguished—the *diffuse* and the *circumscribed*.

In the diffuse form, the whole of the mucous membrane of the body is transformed into a raised nodular mass of growth, generally of soft consistency.

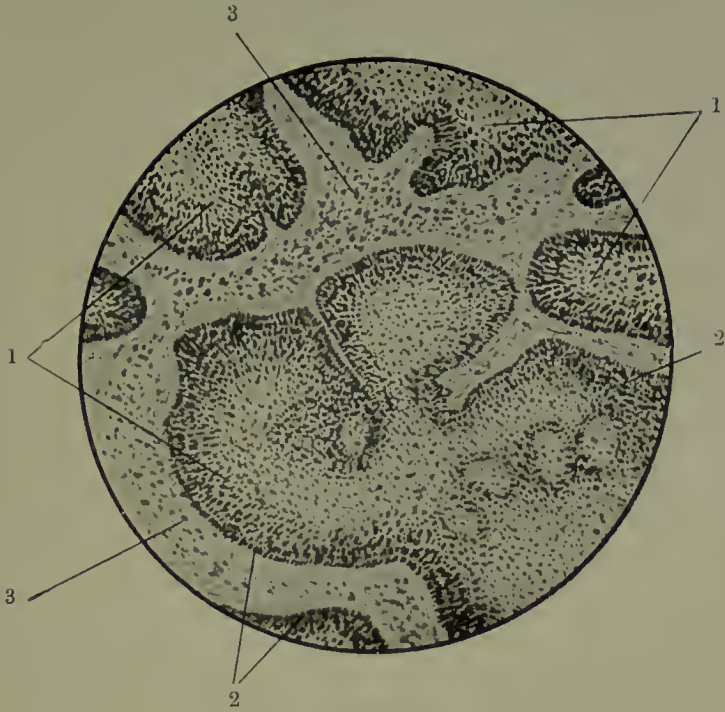
In the circumscribed variety, localised papillary or villous proliferations are met with. Sometimes a cancerous ulcer is found with raised edges, while in very rare cases the disease assumes a distinctly polypoid form.

Carcinoma of the body remains limited to the mucous membrane for long periods, but ultimately it involves the uterine wall, appearing as nodules close under the peritoneal surface. The whole uterus is often greatly enlarged. In other cases, owing to ulceration, the entire mucosa may be destroyed, leading to great attenuation of the uterine wall, and not infrequently to pyometra.

From a histological point of view, by far the most frequent form of growth affecting the body of the uterus is an adeno-carcinoma.

FIG. 23.

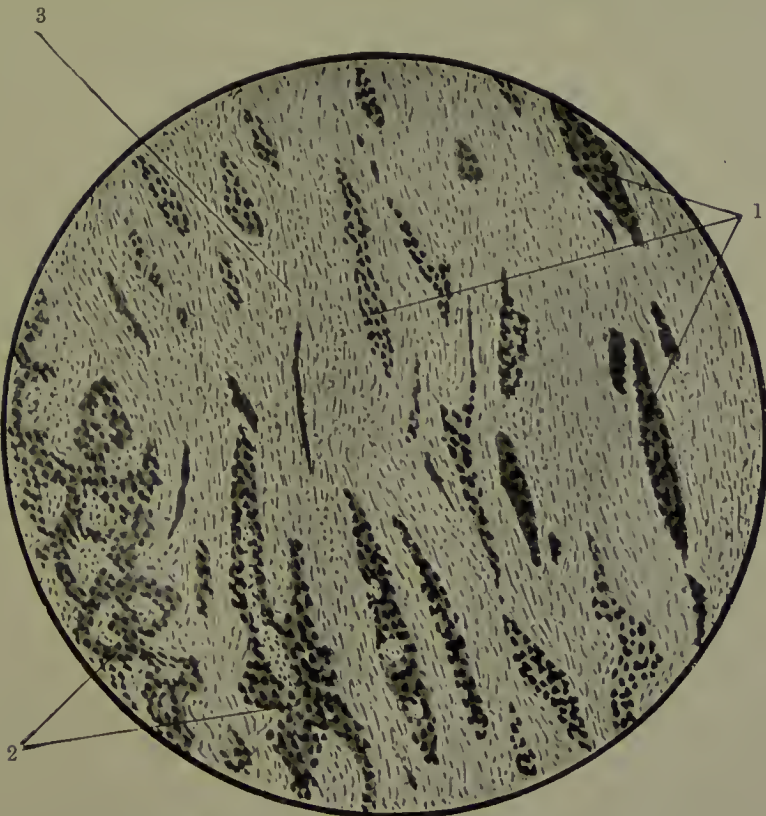
ADENO-CARCINOMA OF THE CERVIX.



1. Solid epithelial cones and nests.
 2. Well marked marginal cylindrical epithelium.
 3. Stroma, infiltrated with small cells.
- (Alum-carmin stain.)

FIG. 24.

CARCINOMA LYMPHATICUM OF THE CERVIX.



1. Narrow bands of epithelial cells within the lymph spaces.
 2. Broader epithelial areas communicating with one another.
 3. Longitudinal muscular bundles.
- (Hæmatoxylin-eosin stain.)

Adenoma malignum, as described above (page 56), may be regarded in many cases as a preliminary stage. The first change observed is an extraordinary increase of the glandular elements with simultaneous atrophy of the interstitial tissue. Next, multi-stratification of epithelium takes place, the cells proliferating inwards as well as outwards, and in the further course of the disease they penetrate deeply into the muscular tissue (fig. 25).

Traces of gland lumina may be seen for long periods, while the proliferating cancer cells frequently maintain their cylindrical shape.

In rarer cases, multi-stratification of the glandular epithelium may at once take place, together with an atypical epithelial proliferation which soon penetrates indefinitely into the surrounding connective tissue and muscular layers.

Squamous-celled epithelioma is of rare occurrence in the body of the uterus. It arises from the mucosa and appears in the form of typical cancrioid or as a horny cancer (Hornkrebs). It either results from a metaplasia of the cylindrical epithelium, or it is a new growth composed of flattened epithelium, this being a further transition stage of the surface cells of the mucous membrane. This has already been observed in connection with carcinoma of the cervix. For differential diagnosis, see page 59.

In conclusion, it must be mentioned that in connection with cancer of the uterus, mixed growths and cancerous degeneration of other forms of tumours may also occur. Among the mixed tumours are chondro-carcinomata and sarco-carcinomata; they are very rare. Among cancerous degenerations myo-carcinoma may be mentioned; this results from the direct extension of carcinoma to a myoma.

(3) SYNCYTIOMA MALIGNUM.—Syncytioma malignum,

also termed chorio-epithelioma, carcinoma syncytiale, deciduoma malignum, &c., is an exceedingly malignant epithelial neoplasm.

In most cases the primary growth occurs in the uterus, and always appears as a concomitant of pregnancy, a confinement, or miscarriage. It may also develop after tubal pregnancy. In a fair number of observed cases syncytioma has occurred after the expulsion of a hydatidiform mole. In the latter case the new growth may arise from any part of the uterine cavity, whereas in other instances the placental site is the starting point. The growth disseminates with remarkable rapidity by means of the blood-vessels, and metastases may occur in distant parts of the body, though they are most frequently found in the vagina and lungs.

Portions of growth removed from the uterus are generally of a soft spongy consistency. On account of their hæmorrhagic character, and since they sometimes occur in a polypoid form, they closely resemble the products of abortion or the remains of placental polypi.

The new growth occurs in the uterus either in the form of a polypoid excrescence with a broad base, or as nodules. These may be either single or multiple, and grow from the wall of the uterus. Their size varies from that of a cob-nut to an apple. The growth is of a soft, friable consistency, and usually has a reddish-brown spongy appearance, containing extensive hæmorrhagic areas, and numerous cavities. It bears a very close resemblance to placental tissue. The secondary nodules are of a similar character. In rare cases, the neoplasm may involve the whole of the uterine wall as a diffuse growth.

Syncytioma malignum from a histological point of view, consists principally of the two different forms of cells which normally cover the chorionic villi, viz., the

FIG. 25.

ADENO-CARCINOMA OF THE BODY OF THE UTERUS.

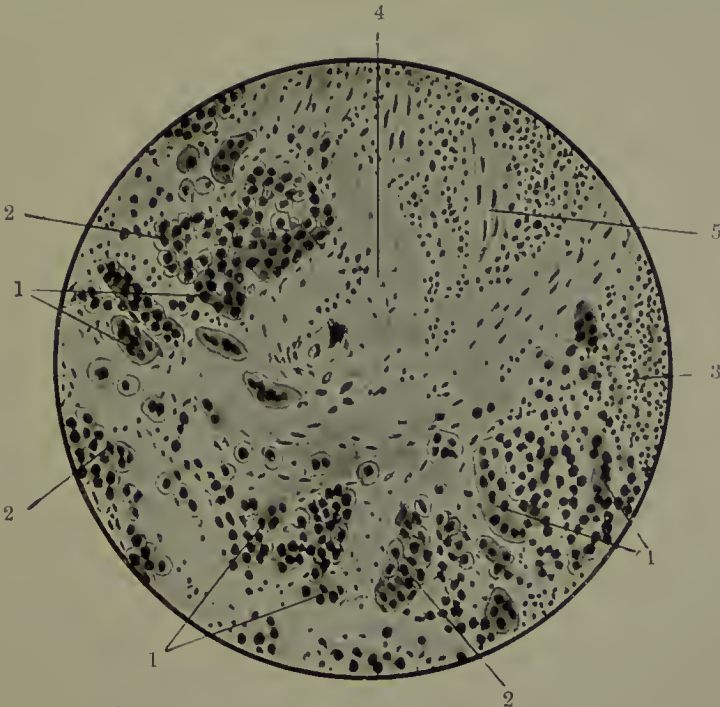


Remains of multi-stratified epithelium of the mucosa, which has for the most part been destroyed owing to necrotic changes. It is seen at one place penetrating into the muscular layers.
 Gland lumina filled with epithelial cells.
 Epithelial nests and cones lying deep in the muscular tissue.
 Normal gland.
 Lumen of vessel.

(Hæmatoxylin-eosin stain.)

FIG. 26.

SYNCYTIOMA MALIGNUM OF THE BODY OF THE UTERUS.



1. Syncytial masses and giant-cells.
2. Langhans' cells.
3. Small-celled infiltration at the edge of the growth.
4. Necrotic areas of connective tissue.
5. Muscular fibres in longitudinal section.

(Hæmatoxylin-eosin stain.)

syncytium, and the cells of Langhans' layer; consequently the chorionic epithelium must be regarded as the actual starting point of the growth. Hardly any regularity can however be perceived in the arrangement of the elements of such proliferation. The two types of cells occur together in confused masses and are frequently surrounded by extensive hæmorrhagic areas, and necrotic, granular, or fibrillary connective tissue (fig. 26). Not uncommonly, the proliferating cells break through the walls of the vessels and entirely fill up their lumen. In the vicinity of such growths an intense small-celled infiltration can frequently be observed.

The tumour cells themselves exhibit wide deviations from their original shape. The syncytium consists partly of long drawn out plasmodia or ribbon-like masses of protoplasm, in which are embedded deeply stained nuclei having no regular arrangement. The protoplasmic masses are sometimes connected by fine processes, in other cases, thick club-like out-growths may appear, in the interior of which vacuoles of varying sizes may be seen.

Besides the larger confluent plasmodial masses, the syncytium may occur in the form of isolated cells, especially giant cells, containing numerous nuclei.

The cells of Langhans' layer, often arranged in group-like form, are found in the vicinity of these syncytial areas, generally enclosed by accumulations of the protoplasm. They are distinguished from syncytial elements by distinct cell outlines and a clear, transparent protoplasm. Their shape is usually similar to that of squamous epithelium, but it may be polygonal. The cells frequently contain several nuclei, and may reach a considerable size. The cells of Langhans' layer moreover frequently show nuclear segmentation figures and glycogenic contents, the wine-red colour of which can be demonstrated by the addition of Lugol's solution.

A typical and an atypical form of syncytioma may be differentiated; in the former case the chorionic epithelium maintains its normal characteristics appearing in the form of communicating protoplasmic areas, while in the latter it occurs as isolated syncytial "wandering cells."

(4) SARCOMA OF THE UTERUS.—Sarcoma of the uterus very rarely occurs in the portio, it is more frequent in the cervix and the body.

(i.) *Sarcoma of the Portio*.—This occurs in the form of polypoid tumours, which as a rule spring from one or other lip of the cervix uteri. It bears a certain external resemblance to ordinary mucous polypi, or even to carcinomatous cauliflower excrescences. Sarcoma occurring as circumscribed nodular tumours in the cervix is less common. Such a growth may be covered with normal mucous membrane.

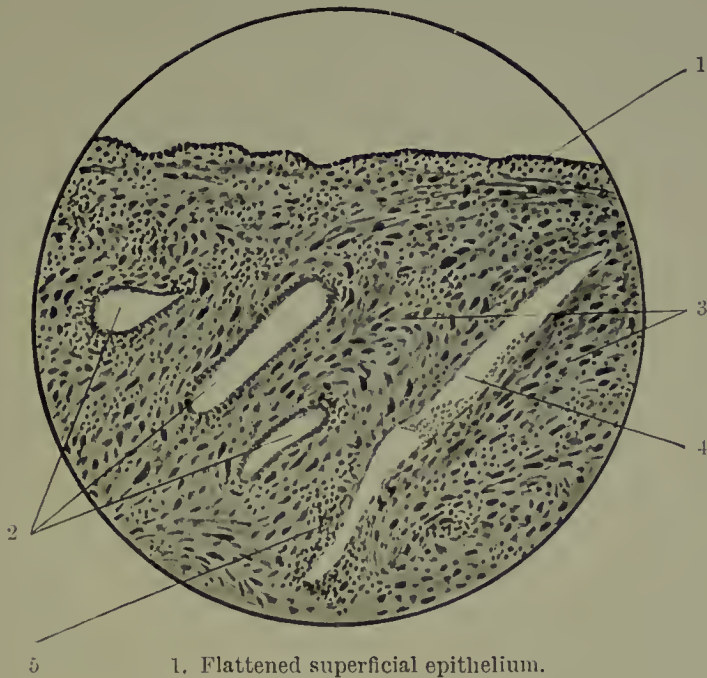
(ii.) *Sarcoma of the Cervix*.—This form of sarcoma has certain definite peculiarities and generally springs from the mucous membrane of the cervix. It appears in the form of lobed polypoid growths which, owing to œdematous infiltration and swelling, may assume a grape-like character (*sarcoma botryoides*). The tumour may also resemble a vesicular mole of the chorion, and often protrudes through the external os into the vagina.

(iii.) *Sarcoma of the Body*.—This is relatively frequent, and may originate either from the mucous membrane or the muscular tissue of the uterus.

Sarcoma of the mucous membrane may be either circumscribed or diffuse. In the first variety, it may form lobed polypoid outgrowths extending widely into the cavity of the uterus, which often undergo superficial ulceration and necrosis. The new growth however does not long confine itself to the mucous surface, but soon involves the muscular walls. It is generally of extremely soft consistency, and on section has a homo-

FIG. 27.

SPINDLE-CELLED SARCOMA OF THE MUCOUS MEMBRANE
OF THE UTERUS.

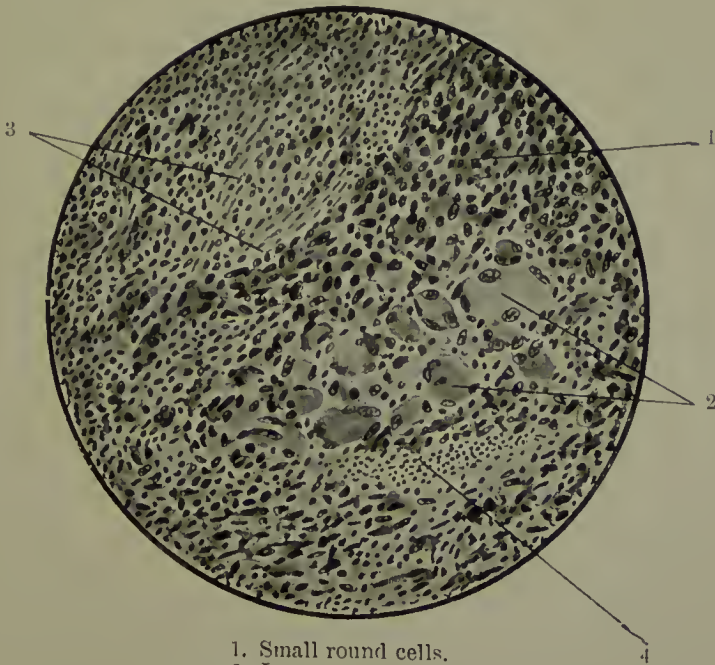


1. Flattened superficial epithelium.
2. Dilated gland-lumina.
3. Spindle-shaped sarcoma cells.
4. Vessel in section.
5. Small-celled infiltration.

(Hæmatoxylin-eosin stain.)

FIG. 28.

ROUND-CELLED AND SPINDLE-CELLED SARCOMA OF THE
UTERINE WALL.



1. Small round cells.
2. Large round cells.
3. Spindle cells.
4. Small-celled infiltration.

(Hæmatoxylin-eosin stain.)

geneous marrow-like appearance. Hæmorrhagic areas are frequently seen in such tumours.

When situated in the uterine wall, pure sarcoma must be distinguished from myo-sarcoma. Myo-sarcoma has a very close resemblance to myoma of the uterus, and may be submucous, interstitial, or subserous. Both sarcoma and myo-sarcoma are found as isolated or multiple growths, though pure sarcoma occurs much more frequently as a single tumour.

On section, pure sarcoma generally has a homogeneous white appearance, while in myo-sarcoma a fibrous arrangement can still be made out.

Both varieties of sarcoma are exceedingly vascular, and contain large blood spaces or extensive hæmorrhagic areas.

Histologically, three principal varieties of sarcoma are met with—spindle-celled, round-celled and giant-celled, though the fact must not be lost sight of that a sarcoma is hardly ever composed of one variety of cell.

Sarcoma generally arises from connective tissue elements, more rarely from muscle, or from the vessel walls.

(*a*) *Spindle-celled Sarcoma*.—In the uterus the spindle-celled variety of sarcoma is common, owing to the fact that sarcomata frequently arise from myomata.* This occurs not only in sarcomata of the uterine wall, but also in those arising from the mucous membrane (fig. 27).

The spindle cells and their nuclei stain very readily, and contain numerous nuclear mitoses. The spindle cells are either arranged in fasciculi crossing one another in all directions, or they may lie irregularly grouped together. In some cases, the cells appear to be arranged concentrically around numerous vascular spaces in the tumour substance.

(*β*) *Round-celled Sarcoma*.—This is usually of soft con-

* This is not in accordance with the Translator's experience, though Orthmann states it as a fact.

sistency and is richer in vessels than the spindle-celled variety. Large round-celled and small round-celled sarcomata occur, but the two varieties may exist together. The former consist of large round cells rich in protoplasm, and frequently containing one or more large vesicular nuclei (fig. 28).

The small round-celled sarcoma consists of small rounded cells with relatively large oval or circular nuclei, surrounded by a narrow border of protoplasm. What is perhaps most striking is the extreme vascularity of such growths, and the frequent extravasations between the cells (fig. 29).

In the vicinity of the vessels, the round cells are noticed in many cases to be more closely arranged; this is probably due to the participation of the adventitia in the new growth. Such tumours are designated angio-sarcomata. The round-celled sarcomata are particularly malignant.

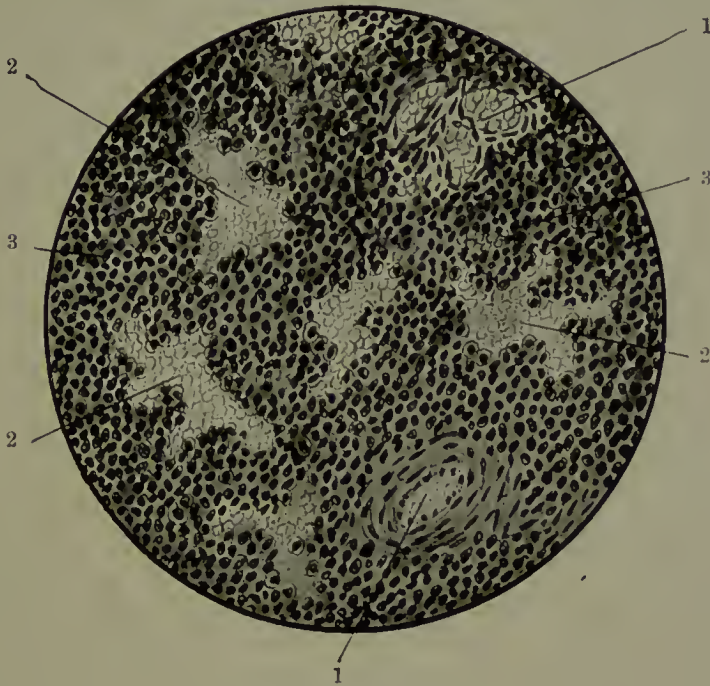
(γ) *Giant-celled Sarcoma*.—This is exceedingly rare, and although isolated giant cells with numerous nuclei are not at all uncommon in spindle-celled and round-celled sarcomata, they must generally be regarded as degeneration products. On the other hand, should the giant cells occur in more definite groups, one is justified in speaking of pure giant-celled sarcoma.

The shape of such giant cells is exceedingly variable, but when occurring in groups they may be more or less similar. The protoplasm is finely granular and stains very readily. The nuclei vary in shape and are irregularly arranged.

A variety of sarcoma is worthy of notice besides angio-sarcoma (sarcoma telangiectoides), which has already been described, viz., alveolar sarcoma. This is distinguished from other varieties by the sarcoma cells being separated from one another by more or less broad vascular septa.

FIG. 29.

ANGIO-SARCOMA OF THE BODY OF THE UTERUS.



1. Blood-vessels in section.
2. Hæmorrhagic areas.
3. Small round cells.

(Hæmatoxylin-eosin stain.)

The most frequent secondary changes in sarcoma are hæmorrhage and necrosis, while extensive fatty, myxomatous, and hyaline changes are not uncommon.

Mixed growths are chondro-sarcoma (which occasionally occurs in the cervix) and carcino-sarcoma. Myo-sarcoma has already been described (page 69).

In conclusion, some mention must be made of endothelioma. This is a rare condition, but it probably belongs to the sarcomata. It arises by a degeneration of the endothelium of the lymphatic vessels and has a distinctly alveolar structure, thus closely resembling a carcinoma. The likeness is still further marked by the fact that the proliferating cells, which originally were spindle-shaped, became transformed into rhomboid cells or large cells resembling squamous epithelium.

In order to confirm the diagnosis a direct proof of the origin of the tumour cells from the growing endothelium of the lymphatic vessels, is necessary.

(D)—DISEASES OF THE FALLOPIAN TUBES.

(1) **Disturbances of Circulation.**

(a) **HYPERÆMIA AND HÆMORRHAGE.**

Owing to the rich blood supply of the tubal mucosa and walls, well marked cases of hyperæmia are met with. Congestive phenomena also occur with diseases of the heart, lungs, liver, and acute fevers, as well as in connection with such local causes as strangulation and torsion.

In hyperæmia, the tube appears swollen and reddened, these changes being especially marked at the fimbriated extremity. Later, free hæmorrhage may occur into the lumen of the tube, while extravasations of blood into the mucous membrane and muscular tissue may lead finally to necrosis.

The most striking changes met with under the micro-

scope are the numerous extravasations of blood amid the folds of the mucosa and the muscular tissue, while the vessels themselves are universally engorged. The connective tissue cells and muscle cells may also be stained with blood pigment.

In well marked cases of hyperæmia of the tube, complete necrosis of the mucous membrane occurs, the cells lose all their staining properties and the vessels undergo extensive hyaline degeneration.

(b) SACTOSALPINX HÆMORRHAGICA (HÆMATOSALPINX).

As a result of atresia of the tube (congenital or acquired) a well marked collection of blood may occur in the tube leading to considerable dilatation. The size of a sactosalpinx hæmorrhagica may reach that of a child's head.

The greatest dilatation of the tube usually occurs at the abdominal ostium, becoming gradually smaller as it approaches the uterus, so that the whole tumour in a way resembles a retort. In hæmatosalpinx the tube is generally thinned, and of a darkish red or bluish-black colour owing to the contained blood.

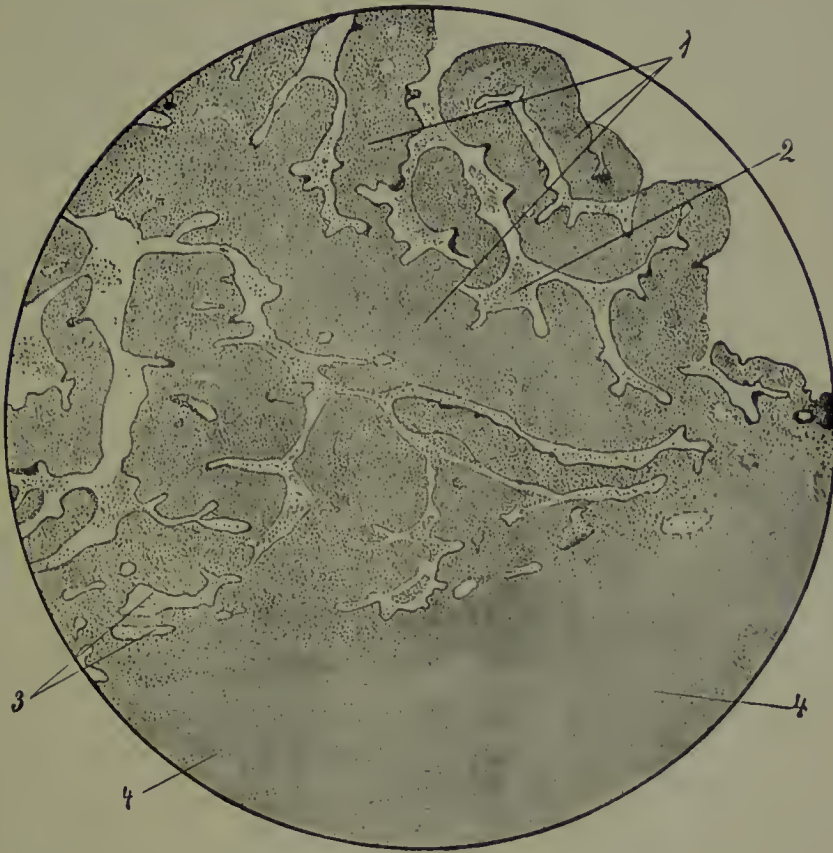
Such tubes generally contain a thick tarry fluid of a dark chocolate-brown colour, and in contradistinction to tubal pregnancy, the blood does not as a rule clot.

The walls of the hæmatosalpinx may at first be of some thickness, but later a well marked thinning takes place, so that rupture easily results from any slight external cause.

Microscopically, the contents consist of degenerate red and white blood corpuscles, epithelial cells, cholesterol crystals, and detritus. The epithelial cells of the mucous membrane and plicæ are preserved for a long period, but in time they become diminished in height and finally assume a flat spindle-like shape. The plicæ become gradually diminished both in height and number,

FIG. 30.

CHRONIC CATARRHAL SALPINGITIS.



1. Thickened plicæ showing small-celled infiltration.
2. Mucoid material between the folds of mucous membrane, containing many round cells.
3. Lacunæ of the mucous membrane sequestered in the deeper tissues of the tube wall.
4. Muscular wall infiltrated with small cells.

(Hæmatoxylin-eosin stain).

and contain numerous dilated vessels and hæmorrhagic extravasations. The muscular tissue, which is at first thickened, after a time becomes stretched and thinned by the contained blood, and areas of round-celled infiltration occur in the neighbourhood of the peritoneal coat. This is also noticeable in the region of the vessels. On the peritoneal surface abundant fibrinous deposits occur, and near the abdominal ostium well marked adhesions and bands are frequently met with.

(2) Inflammation of the Tube, and Infective Granulomata.

(a) INFLAMMATION.

Inflammation of the Fallopian tube may be either catarrhal or purulent, though it is often impossible to draw a sharp distinction between the two. Both forms have an acute and a chronic stage. In the latter, characteristic changes arise which gradually cause occlusion of the abdominal end and retention of the inflammatory secretions. Such a condition may be designated as Sactosalpinx, and according to its contents, sactosalpinx serosa (hydrosalpinx), sactosalpinx hæmorrhagica (hæmatosalpinx), and sactosalpinx purulenta (pyosalpinx) may be recognised.

Etiologically, micro-organisms play a very important part in inflammation of the Fallopian tube; those most frequently met with being gonococci, streptococci, staphylococci, pneumococci, and the bacillus coli communis.

(I) CATARRHAL SALPINGITIS.—In the acute stage the secretion is thin, fluid in character, and much increased in amount; later, it becomes mucoid and thick, and contains numerous leucocytes, red blood corpuscles, and fatty, mucoid, or hyaline epithelial cells.

Owing to its increased vascularity the tube is often thickened and reddened, especially at the fimbriated end.

Later, the tube becomes markedly tortuous, the walls adhere together, and as a result of peritoneal inflammation, the abdominal ostium may become completely closed.

Microscopically, the inflammatory changes are most marked in the connective tissue of the plicæ, but the epithelium may remain unchanged for a long period. The vessels of the mucosa are seen to be injected and increased in number, and the lymph spaces are frequently dilated.

As a rule the summits of the plicæ show a well marked, small-celled infiltration which gradually involves other portions, and leads to a general swelling and thickening (fig. 30).

In chronic cases, distinct atrophy of the superficial epithelium of the plicæ may be noted, whilst adhesions of neighbouring folds to one another may give rise to a sequestration of the deeper lying portions of the mucous membrane, so that cavities of varying size occur in this situation lined with definite epithelium. As a result of an increase in their secretion, these cavities become dilated and form small multiple cysts, giving to the mucosa of the tube a cribriform or sieve-like appearance on transverse section. This condition is termed salpingitis pseudo-follicularis (fig. 31).

In the later course of catarrhal salpingitis the muscular layers are also affected. In the neighbourhood of the vessels collections of round cells are numerous, whilst the muscular bundles as well as the connective tissue become hypertrophied.

Finally, the inflammatory processes may reach the peritoneal coat, which becoming covered with lymph, results in a matting together of the folds and adhesion of the tube to neighbouring organs.

Special varieties of catarrhal salpingitis are termed salpingitis hæmorrhagica, and salpingitis isthmica nodosa.

FIG. 31.

SALPINGITIS PSEUDO-FOLLICULARIS.



1. Lumen of the tube.
2. Thickened knob-like folds of the mucosa infiltrated with small round cells.
3. Muscular layer infiltrated with small round cells.
4. Remains of the original epithelium of the plicae.
5. Sequestered areas of mucous membrane.
6. Dilated and cystic cavities resembling follicles in the deeper layers of the mucosa.
7. Well marked area of round-celled infiltration in a fold of the mucosa.

(Hematoxylin-eosin stain.)

Salpingitis hæmorrhagica is characterised by mixture of the catarrhal secretions with blood, and extensive hæmorrhages amid the mucous folds.

In *salpingitis isthmica nodosa*, nodular thickenings of the tube walls are seen in the neighbourhood of the uterine end. These changes result from chronic inflammatory processes, and are produced by a circumscribed muscular hyperplasia occurring round sequestered portions of the mucous membrane.

(2) SACTOSALPINX SEROSA (HYDROSALPINX), AND SACTOSALPINX HÆMORRHAGICA (HÆMATOSALPINX).—Hydrosalpinx is probably one of the stages of chronic catarrhal salpingitis. If the clear serous contents become mixed with blood, or should hæmorrhage occur into the tube such a condition may be termed hæmatosalpinx.

Hydrosalpinx or hæmatosalpinx may vary in size from that of a finger to a child's head. They are shaped like a club or retort, the greatest dilatation occurring at the occluded ampullary portion.

The tubal walls, from increase of their contents may in some cases become extraordinarily thin, and are frequently covered with peritoneal adhesions. The occluded abdominal ostium is often only indicated by a radiate or stellate scar. The folds of the mucous membrane become diminished in height and separated from one another as the result of internal fluid pressure.

Finally, they lose their original shape and only appear as projections on the inner surface of the tube. Should a hydrosalpinx open into an ovarian cyst a tubo-ovarian cyst results.

Microscopically, the most varied inflammatory changes are found both in the mucous membrane and the muscular layers.

It is a curious fact that the epithelium of the plicæ is preserved for a long time though considerably altered, and even well marked ciliated epithelial cells

are met with. The folds of the mucous membrane become gradually lessened in height, while deep in its substance numerous sequestered mucous cavities occur (fig. 32). At times small papillary proliferations of the mucosa may be seen projecting into the lumen of the tube.

The muscular layers also atrophy and in the end almost disappear, so that the tube wall consists only of thin fibrous connective tissue with a few vessels here and there.

The contents of a hæmatosalpinx consist chiefly of red blood corpuscles and their degeneration products. Sometimes fibrin coagula and degenerated epithelial cells are met with. The folds of the mucosa are infiltrated with blood pigment, while hæmorrhagic extravasations may be seen in the muscular layers.

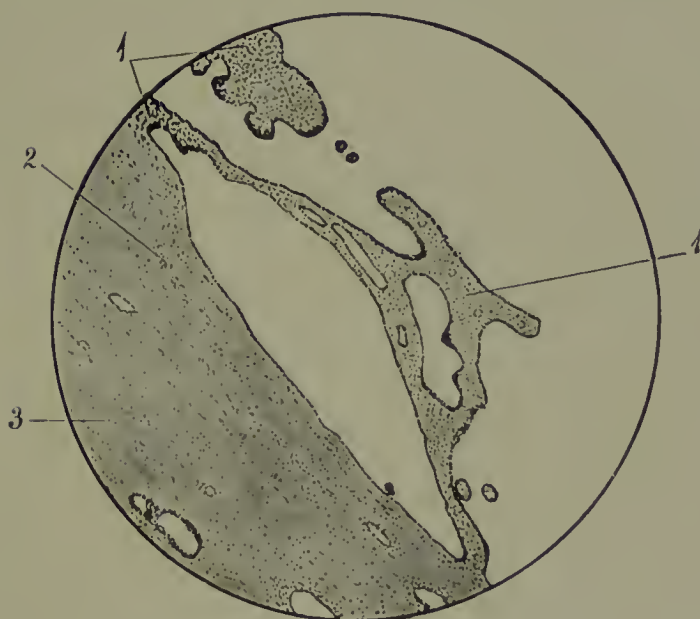
(3) SALPINGITIS PURULENTA.—In acute purulent salpingitis the peritoneal coat is at first much congested as a result of the intense engorgement and dilatation of the vessels, while in places fibrinous lymph deposits occur which later form definite adhesions. The walls of the tube are thickened and œdematous, the folds of the mucosa especially at the fimbriated extremity being much injected, swollen, and covered with purulent secretion.

In chronic cases, the tube becomes tortuous and folded upon itself in a remarkable manner, the folds often adhering to one another. The walls at the same time are often much thickened and indurated. The contents usually consist either of pus or caseous material. The folds of the mucosa are at first thickened and swollen, becoming gradually lessened in height, and finally flattened out against the tube wall. Sometimes, small abscess cavities occur within the thickened muscular layers.

Microscopically, it is very important that a bacterial

FIG. 32.

SACTOSALPINX SEROSA (HYDROSALPINX).



1. Remains of the folds of the mucosa, much compressed and adherent to one another.
2. Atrophied muscular bundles.
3. Fibrous layers of the tube wall.

(Van Gieson's stain.)

examination should be made of the contents of such tubes, for in this way some conclusion may be arrived at as to the etiological factors of the disease. The organisms most frequently found are gonococci, streptococci, and staphylococci; these may occur not only in the pus but in some cases in the mucus membrane or muscular layers.

In the earlier stages of purulent inflammatory changes of the tube it is almost always possible to come to a definite conclusion histologically as to the etiology of the disease, but later, these histological distinctions are wanting, and it may be impossible to discover any characteristic bacteria in the purulent secretion of such tubes.

Gonorrhœal salpingitis must be distinguished from non-gonorrhœal. Gonorrhœal salpingitis is especially at first confined to the mucous membrane which is reddened and swollen, while the summits of the mucous folds are infiltrated by numerous collections of small round cells. In the non-gonorrhœal form, the lymphatic vessels are chiefly affected. This is seen especially in acute infective processes occurring after labour and abortion. In such cases the whole tubal wall is affected, while considerable dilatations of the lymph spaces occur in the mucous membrane containing either serous or purulent fluid. The blood-vessels in the summits of the plicæ are extraordinarily injected, and very numerous.

The epithelium itself resists the inflammatory changes for a long period. The cilia at first disappear, while as a result of internal pressure the mucous folds become diminished in height.

The superficial portions of the swollen mucosa, infiltrated with leucocytes, may finally completely disappear owing to further purulent destruction (fig. 33), though in the deeper recesses of the mucosa remnants of unaltered mucous membrane may remain for a very long

time. Owing to areas of the mucosa being denuded of epithelium, adhesions between the thickened club-like plicæ soon form. The muscular layers are likewise infiltrated with small round cells, which are seen amid the compressed muscular bundles either in small rounded collections or in continuous tracts. In chronic cases, the contents of such tubes assume a thick cheesy appearance, the number of bacteria diminishing according to the length of duration of the disease.

In places the superficial epithelium may still preserve its original form, but usually it is diminished in height, and becomes cubical or spindle-celled in appearance. Deeper still in the mucosa however, numerous gland-like spaces occur lined with epithelium which result from adhesions of the folds and plicæ of the mucous membrane (fig. 34).

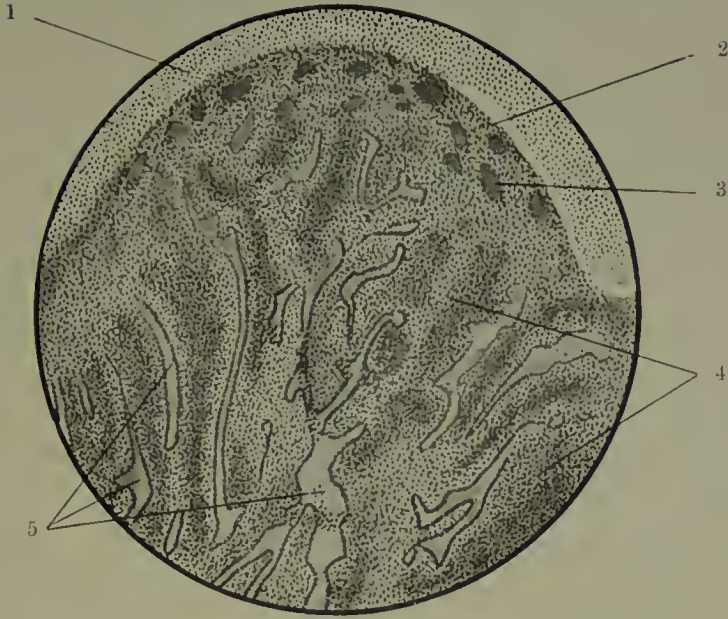
As a result of such adhesion of the densely infiltrated mucous folds, the lumen of the tube often becomes separated into numerous loculi. Later, the mucosa may become diminished in height and atrophied, and at length the destructive processes may involve the muscular coat, which is now only covered with wide areas of granulation tissue. Sometimes the muscular layer of the tube wall becomes extraordinarily thickened, due mostly to hyperplasia of the intermuscular connective tissue, amid which areas of round-celled infiltration, small abscess cavities, and dilated vessels with thickened walls, are met with.

(4) SACTOSALPINX PURULENTA (PYOSALPINX).—One of the results of chronic purulent salpingitis, with its accompanying perisalpingitis, is a closure of the abdominal end of the tube.

This gives rise to pyosalpinx. The size of such tubes may vary from that of a finger to that of a closed fist, or even a child's head. The tube walls vary in thickness, and although considerable hypertrophy may occur,

FIG. 33.

ACUTE PURULENT SALPINGITIS.

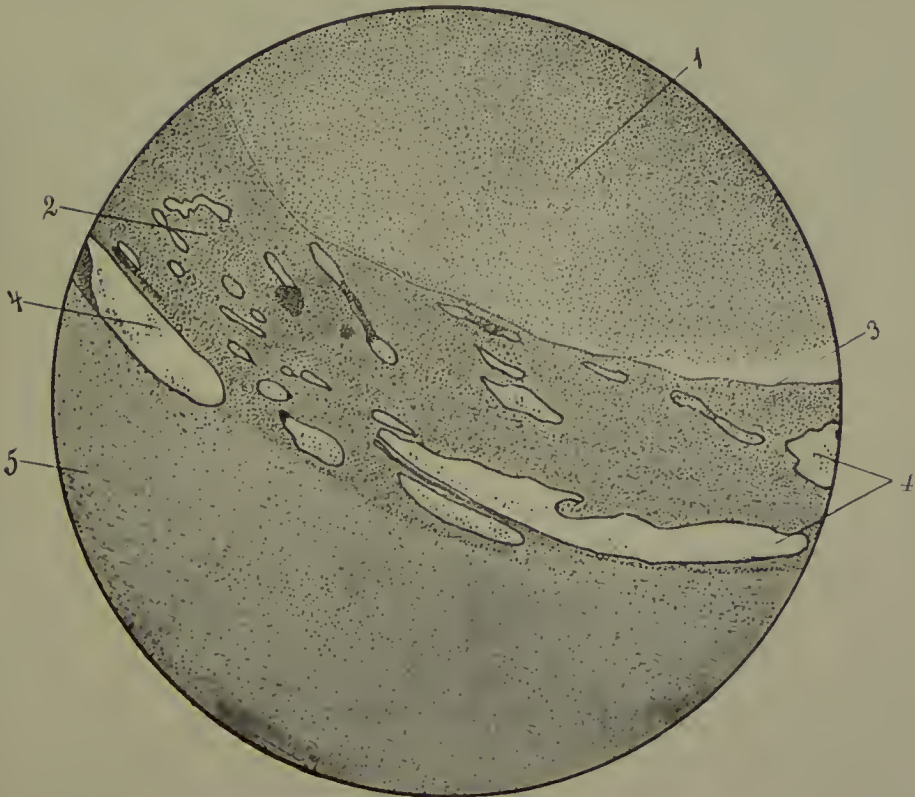


1. Lumen of tube filled with pus.
2. Thick swollen mucosa, destitute of epithelium.
3. Injected vessels near the surface of the mucous folds.
4. Well-marked small-celled infiltration of the stroma.
5. Sequestered and compressed gland spaces.

(Hæmatoxyliu-eosin stain.)

FIG. 34.

CHRONIC PURULENT SALPINGITIS.



- | | |
|--|--|
| Lumen of tube filled with pus. | 4. Sequestered and compressed gland-like spaces. |
| Much compressed folds of mucous membrane. | 5. Muscular layer infiltrated with small cells. |
| Superficial epithelial layer much flattened. | |

(Hæmatoxylin-eosin stain.)

purulent destruction may eventually lead to thinning of the wall. The tube contains either thin or thick pus, in which only a few micro-organisms can be found.

The folds of the mucosa may only be represented by small eminences or a few scattered folds, which sometimes project into the lumen for some distance (fig. 35). The peritoneal coat is generally covered with numerous thick adhesions, and the mesosalpinx is markedly œdematous. If a pyosalpinx communicates with an ovarian abscess a so-called tubo-ovarian abscess results.

Microscopically, the superficial epithelium may at times appear fairly well preserved, the plicæ and folds being merely infiltrated with small cells and containing injected vessels; in other cases hardly any trace of the mucosa remains. Here and there, close to the muscular layers, small gland-like cavities lined with epithelium are seen as remnants of the original mucous membrane. In the end the mucosa is merely represented by a scanty layer of granulation tissue, or fibrous indurated cicatricial connective tissue.

The muscular fibres are generally atrophied, and separated by hyperplastic connective tissue, while not infrequently the whole wall is very œdematous.

The vessels, especially in the neighbourhood of the peritoneal coat, are increased in number, and often show evidence of hyaline degeneration. The peritoneal surface is frequently covered with dense adhesions.

(b) INFECTIVE GRANULOMATA.

Among infective granulomata of the Fallopian tube, leprosy, syphilis, actinomycosis, and tubercle, have been observed. The three first are extremely rare, but tubercle occurs with sufficient frequency to deserve notice.

TUBERCULOUS SALPINGITIS.—Tuberculosis of the tube may be either primary or secondary; the first is

usually a chronic disease, while the latter may often occur in an acute form.

In its early stages tuberculous salpingitis cannot be distinguished from the ordinary catarrhal variety. The tube is thickened and tortuous, and contains a mucoid or cheesy secretion; later, small grey miliary tubercles may be seen in the much thickened mucosa. The tubercles are most frequent in the region of the ampulla. The scattered tuberculous nodules soon become confluent and break down, and the whole mucosa becomes covered with caseous necrotic patches. The cheesy material may eventually completely occlude the tube. The disease may further invade either the muscular layers or the peritoneal covering, the latter sometimes being studded with tuberculous nodules.

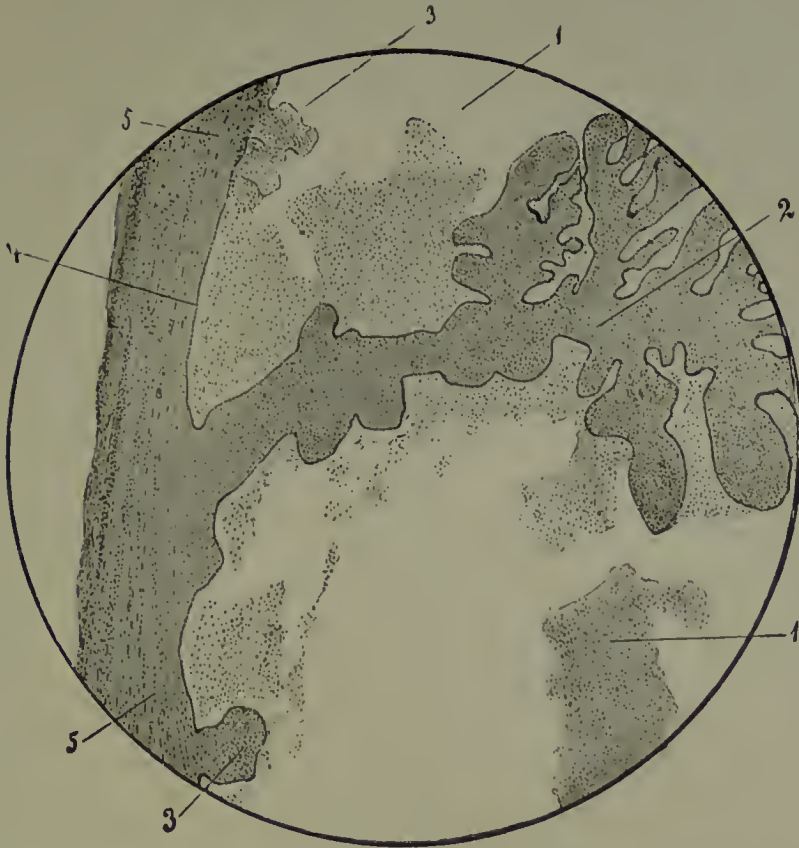
Tubercle in its chronic form nearly always leads to a closure of the abdominal end of the tube, thus forming a tuberculous sactosalpinx which may reach a considerable size, some cases being as large as a child's head. The tubal walls are usually much hypertrophied, and small tuberculous projections often occur in the mucous lining. The muscular layers are sclerosed, and in the region of the isthmus nodular swellings are sometimes seen which correspond to small caseous abscesses. The peritoneal coat is much thickened and is covered with tuberculous nodules.

Microscopically, the acute and chronic forms of tubercle exhibit distinct differences. In the acute variety the tube generally contains cheesy masses of detritus in which numerous bacilli are found. The mucosa at first shows evidence of acute catarrh with numerous areas of round-celled infiltration and tuberculous nodules, the latter containing characteristic giant cells; later, caseous changes set in which may involve the mucosa and peritoneal coats.

In chronic cases, the tube frequently contains pus, the plicæ are much thickened and everywhere infiltrated

FIG. 35.

SACTOSALPINX PURULENTA (PYOSALPINX).



- | | |
|--|--------------------------------------|
| 1. Lumen of tube filled with pus. | 3. Atrophied fold of the mucosa. |
| 2. Long, well preserved, branching fold of the mucosa. | 4. Flattened superficial epithelium. |
| | 5. Much atrophied muscular coat. |

(Hæmatoxylin-eosin stain.)

FIG. 36.

CHRONIC TUBERCULOUS SALPINGITIS.



- | | |
|---|---|
| Muscular layer of the tube. | 4. Tuberculous nodules, with large giant-cells. |
| Sequestered gland-like areas of the mucosa. | 5. Isolated giant-cells. |
| Mucosa infiltrated with small cells. | |

(Hæmatoxylin-eosin stain.)

with numerous tuberculous nodules containing large giant cells. The superficial epithelium is soon lost, the plicæ become glued together, and finally the mucosa is only represented by mere granulation tissue. For a time, however, deep in the mucosa a few sequestered gland-like spaces lined with epithelium can be made out (fig. 36). Here and there in the mucous folds proliferations of included epithelial remains may sometimes be observed, as well as metamorphoses of the epithelium of the giant cell areas.

As a rule in these cases tubercle bacilli are not very numerous, but in the early stages they occur inside the giant cells. Later, the whole mucosa may undergo caseous degenerative changes, and the muscular layers as well as the peritoneal coat contain numerous tuberculous nodules. The former are affected with a diffuse round-celled infiltration and hyperplasia of the intermuscular connective tissue. The peritoneal coat shows thickened tuberculous patches containing numerous giant cells.

(3) New Growths.

(a) INNOCENT NEW GROWTHS.

(1) CYSTS.—True cystic new growths of the tube are extremely rare, although cystic formations having an inflammatory origin, such as hydro-salpinx, salpingitis pseudo-follicularis, and peri-salpingitis, are common enough.

To this class also belong cystic structures arising from accessory tubes (Nebentuben). Their walls consist of thin connective tissue while here and there, especially in the pedicle, unstriated muscle is met with. Their inner wall is sometimes lined with ciliated cylindrical epithelium (hydro-parasalpinx).

Such cysts may arise from any part of the tube wall,

or may occur between the layers of the broad ligament. Occasionally cysts representing dilated lymph spaces occur in the peritoneal covering of the tube, and are lined with characteristic endothelium.

Finally, the hydatid of Morgagni is sometimes considerably enlarged, reaching the size of a walnut or an apple.

(2) MUCOUS POLYPI OF THE TUBE.—True mucous polypi of the tube occur only very rarely, in spite of the peculiar folded construction of the mucous membrane. These folds can easily be mistaken for polypoid proliferations of the inflamed mucosa, but in the latter case accompanying inflammatory changes can be recognised. Sessile polypi of the mucous membrane occurring in the isthmus of the tube may block the lumen, and by preventing the onward passage of a fertilised ovum, lead to a tubal pregnancy.

The microscopic structure of mucous polypi corresponds exactly to that of hypertrophied mucous membrane. They consist of a loose connective tissue stroma and are covered by ciliated epithelium, which however is of a lower type than normal.

(3) PAPILLOMA.—These tumours also belong to the innocent new growths of the tubal mucous membrane. Two main varieties can be distinguished, viz., the simple, and the cystic papilloma.

The *simple* papilloma occurs either as a soft or sometimes as a hard cauliflower-like papillary tumour, arising from the mucosa. It may completely fill the lumen of the tube and may sometimes considerably distend it. The new growth never penetrates the muscular layers, but may on the other hand sprout from the abdominal ostium and give rise to ascites. It may occur in conjunction with papilloma of the ovary.

Microscopically, papilloma of the tube consists of numerous wide branching proliferations of the mucous membrane, which sometimes adhere to one another.

The stroma is formed of connective tissue containing numerous cells, and in the club-shaped thickened papillæ it is hyaline in character. The epithelium on the summits of the altered papillæ may in some cases consist of ciliated cylindrical cells of varying height. It is always single layered.

Cystic papilloma of the tube consists of vesicular proliferations of the mucous membrane and closely resembles a hydatidiform mole. These sometimes sprout in numerous grape-like masses from the fimbriated end of the tube.

Microscopically, they consist of a rich cellular connective tissue stroma and are covered with ciliated cylindrical epithelium. The stroma of the summits of the papillæ contains numerous small cystic cavities. These cavities are lined with cylindrical epithelium, and on their inner surface small papillary growths are met with. Papillary growths may also occur on the peritoneal coat of the tube.

(4) CONNECTIVE TISSUE NEW GROWTHS. — Innocent connective tissue tumours of the tube are very rare, but myoma and fibroma occur. They arise from the muscular layers of the tube wall, and consist of diffuse unencapsuled swellings within the muscular tissue. They sometimes reach the size of a cherry-stone or a small apple.

Microscopically, they consist of bundles of unstripped muscle and connective tissue. The occurrence of epithelial inclusions in such tumours lends colour to the theory that they arise from accessory Müllerian ducts. They are really adeno-myomata.

A pedunculated multiple fibro-myomatous tumour has been observed springing from the fimbriated end of the tube containing cystic spaces destitute of epithelium. These apparently originated from myxomatous degeneration of the tumour.

(b) MALIGNANT NEW GROWTHS.

(1) CARCINOMA.—Carcinoma of the Fallopian tube may be either primary or secondary, the latter generally occurring in connection with carcinoma of the ovary or body of the uterus.

Primary carcinoma always arises from the mucous lining of the tube. Two forms occur—the circumscribed nodular, and the diffuse papillary variety. In external appearances such tubes are very like those due to inflammatory changes, and the abdominal ostium is frequently occluded. When the muscular wall is completely infiltrated with the growth, the peritoneal coat may be bulged forward, and the tumour may then have a sausage-shaped nodular appearance. Such tubes sometimes attain the size of a fist or even a child's head. On section numerous protruding papillary proliferations are seen in the interior, and even in the nodular variety of carcinoma the greater part of the tube may be filled with new growth. These nodular tumours may reach the size of a pigeon's egg or a fist; they are of the consistency of marrow and on section are more or less yellow in appearance.

Secondary carcinoma of the tube may also occur in a circumscribed or a diffuse form. Extension of cancerous nodules from the ovary to the tube has been observed.

Microscopically, carcinoma of the tube occurs in two different forms, which may be compared to malignant adenoma and adeno-carcinoma of the body of the uterus. At the same time it should be remembered that the type of primary tubal carcinoma is papillary and not adenomatous, and since the normal tube is really destitute of glands, adenoma or adenomatous tumours of the tube cannot, as such, occur.

The first variety of carcinoma of the tube may be termed *carcinoma papillare simplex*. It is, as its name

FIG. 37.

PAPILLARY ALVEOLAR CARCINOMA OF THE TUBE.



1. Papillary proliferations of the mucosa covered with many layers of epithelium.
2. Solid epithelial masses.
3. Cancerous alveolus deep in the muscular tissue, containing papillary elevations of the epithelium.
4. Muscular tissue close beneath the mucosa.

(Hæmatoxylin-eosin stain.)

FIG. 38.

PAPILLARY CARCINOMA OF THE TUBE.

Showing Epithelial Metamorphoses (Metaplasia).



1. Papillary epithelial proliferation.
2. Sequestered areas of the mucosa lined with many layers of cylindrical epithelium.
3. Nests of squamous cells lying within the mucous membrane, due to metaplasia of cylindrical epithelium.

(Hæmatoxylin-eosin stain.)

denotes, a purely papillary growth. Its microscopic structure is seen to consist of long irregular interwoven papillæ, provided with a single layer of cylindrical epithelium. The stroma is scanty, and only contains a few cells. The malignant character of these papillæ however is evident from the fact that they grow inwards towards the muscular coat and eventually involve the whole wall of the tube.

The second variety assumes an alveolar type, and is termed *carcinoma papillare alveolare*. The growth consists of numerous papillary proliferations of the mucous lining of the tube. At first these are covered by a single layer of cylindrical cells, but after a time they become many-layered and grow not only towards the lumen but extend in solid plugs into the deeper strata of the mucosa and muscular tissue in all directions (fig. 37). These plugs of epithelial cells may become isolated amid the connective tissue stroma or in the muscular layers, thus giving a well marked alveolar appearance to the new growth.

Secondary hyaline degeneration occurs in carcinoma of the tube, and as in carcinoma of the body of the uterus, a transformation of the cylindrical epithelium into squamous epithelium may take place.

The accompanying drawing (fig. 38), from a case of primary papillary alveolar carcinoma of the tube, shows numerous groups of squamous epithelial cells which result from a direct transformation of the proliferated many-layered cylindrical epithelium of the mucosa.

Whilst carcinoma papillare simplex is said to occur most frequently, out of five cases of carcinoma of the tube observed by Orthmann [of which three were primary and two secondary to carcinoma of the ovary] the alveolar type was always found.

The secondary carcinomata of the tube resemble in all respects the primary growths.

(2) **SYNCYTIOMA MALIGNUM.** — Following upon tubal pregnancy a malignant new growth may develop in the tube, arising from the epithelium of the chorionic villi. It is mostly made up of the cells of the syncytium and Langhans' cells, and corresponds to syncytioma malignum of uterine origin (see page 65).

(3) **SARCOMA.**—Sarcoma of the Fallopian tube is rarer than carcinoma and may occur either primarily or secondarily. Sarcoma of the mucous membrane must be differentiated from that arising in the wall. Both may be either diffuse or circumscribed; in the latter, the sarcoma occurs in a nodular form, while in the former it is usually papillary. The whole tube in such cases is thickened, and on section the growth has a homogeneous marrow-like appearance. The tumour may spread through the whole wall and involve the peritoneum, forming nodular outgrowths on its surface.

Microscopically, sarcoma of the Fallopian tube may be either of the round or spindle-celled variety. In some cases the epithelial cells of the mucosa of the tube undergo proliferative processes, in others, the whole mucosa is infiltrated with sarcoma cells. The superficial epithelium generally remains unchanged, or is only slightly compressed (figs. 39, 40,).

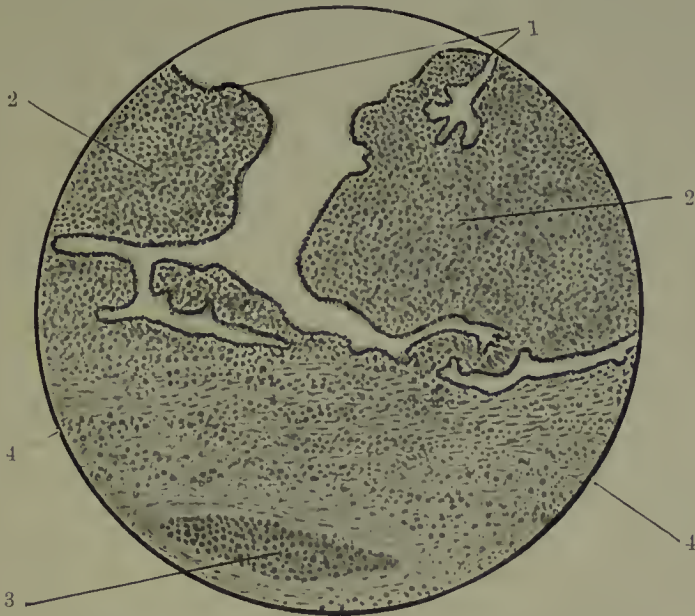
In secondary sarcoma of the tube the growth appears to first attack the muscular layers by means of the lymph channels, and then to spread through the mucous membrane. All the lymph channels are enormously dilated and crowded with sarcomatous cells. Small round-celled sarcoma occurs most frequently.

(4) **Tubal Pregnancy.**

Of all forms of ectopic foetation, tubal pregnancy is the most frequent. Three principal varieties can be distinguished:—interstitial, isthmic, and ampullary. A further division may be made into tubo-uterine, tubo-ovarian, and tubo-abdominal.

FIG. 39.

ROUND-CELLED SARCOMA OF THE MUCOUS MEMBRANE AND MUSCULAR LAYERS OF THE TUBE. Secondary to Sarcoma of the Ovary.



1. Compressed, but otherwise normal superficial epithelium.
2. Small round-celled sarcoma of the mucous membrane.
3. Lymph channels packed with sarcoma cells.
4. Degenerate muscular layers infiltrated with sarcoma cells.

(Hæmatoxylin-eosin stain.)

FIG. 40.

ROUND-CELLED SARCOMA OF THE MUCOUS MEMBRANE OF THE TUBE.

(From a portion of the growth shown in Fig. 39 more highly magnified.)



1. Somewhat flattened superficial epithelium, partly cylindrical, partly cubical in shape.
2. Round-celled sarcoma cells replacing the stroma cells.

(Hæmatoxylin-eosin stain.)

Abdominal and intra-ligamentous pregnancy occur as a result of secondary changes. Very rarely the ovum has been observed growing amid the fimbriæ.

In a very large number of cases the ovum perishes as the result of rupture of the tube or tubal abortion, especially during the first four months. Rupture seems to occur more frequently in the interstitial and isthmic varieties, while abortion is the rule in the ampullary form. In rare cases rupture of the tube and tubal abortion may occur at the same time.

The immediate result of tubal rupture or abortion is hæmorrhage from the rent in the tube, or from the placental site. Diffuse hæmorrhage may occur into the peritoneal cavity or the blood may be localised, leading to the formation of a retro-uterine hæmatocele or to a hæmatoma of the broad ligament.

As a result of interruption of a tubal pregnancy the fate of the foetus varies according to its age; in the early months it may be completely absorbed, but in the later mummification or maceration may occur.

On naked-eye examination, in the interstitial and isthmic varieties, the tube is distended and filled by a firm blood clot which often gives a bluish-black appearance to the tumour. The walls of the tube eventually become extraordinarily thinned, and finally rupture of the peritoneal coat occurs.

In the ampullary variety the ampulla is more or less dilated and occupied by a round or oval mass of blood-clot, which may partly hang out of the fimbriated extremity of the tube.

In all cases of interrupted tubal pregnancy coagulated organised blood-clot is found in the interior of the tube, while in hæmatosalpinx the blood remains fluid.

If the blood-clot in tubal pregnancy be laid open an irregularly-formed smooth-walled space is frequently seen in its interior, the true amniotic cavity, in which a foetus is sometimes lodged.

The microscopical examination of the products of interrupted tubal pregnancy is therefore of great importance in order to determine either from the blood-clot alone, or from the changes in the tube, whether a pregnancy really has ever existed. The foetus in such cases has often disappeared.

The presence of chorionic villi is very important. The proof of the existence of decidual cells is a more difficult matter, for they have much less power of resistance and during the early months are only to be found in the immediate neighbourhood of the ovum.

Chorionic villi are usually found in the greatest number in the region of the attachment of the ovum to the tube, and are quite easily recognised by their double epithelial layer and loose connective tissue stroma (fig. 41). In the blood clot, chorionic villi present a somewhat different appearance; they may be considerably longer than normal, the syncytium is often wanting, and only the much flattened layer of Langhans' cells can be made out. The villi in such cases are frequently the seat of necrotic changes, and are often surrounded by rings of canalised fibrin.

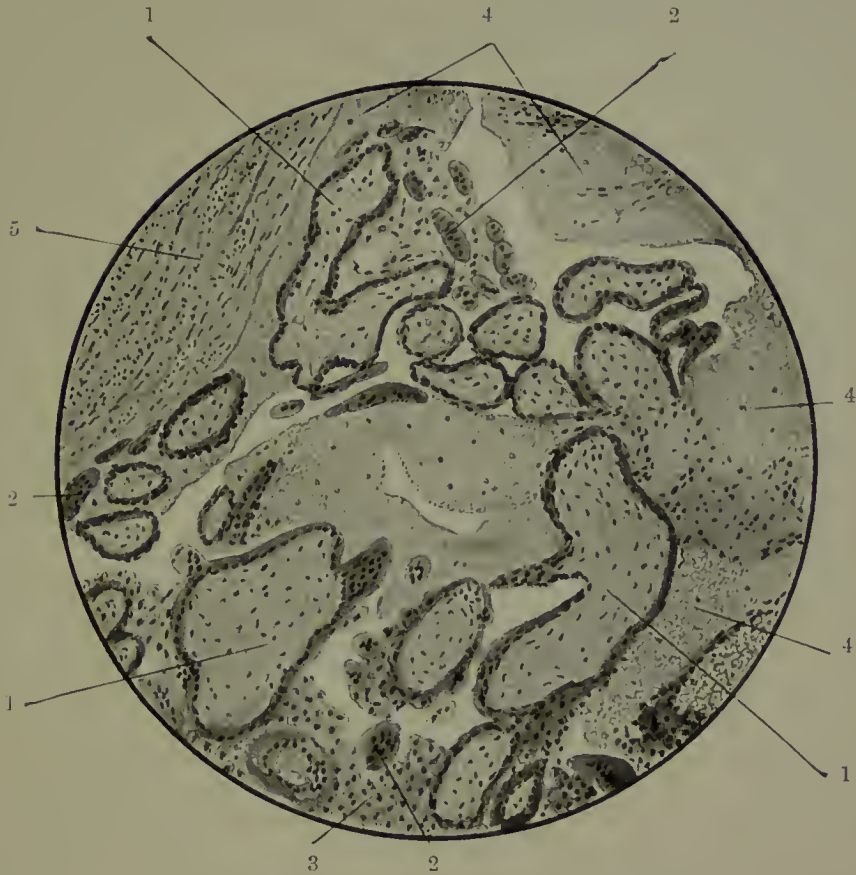
The decidual cells in ectopic pregnancy are formed from the connective tissue cells of the stroma of the mucosa, and are most frequently seen at the summits of the mucous folds. The form and size of such decidual cells correspond exactly to those of the uterine decidua.

The decidual formation appears to be more extensive as the pregnancy advances, the whole mucous membrane of the tube being eventually changed into a decidua (fig. 42). The epithelium of the mucosa may exhibit syncytial characters in those parts where decidual cells occur.

In tubal pregnancy, as in an ordinary uterine pregnancy, a decidua vera, serotina (basal), and reflexa (capsular) are found. The muscular layers of the tube are

FIG. 41.

(ISTHMIC) TUBAL PREGNANCY. (Ruptured at the second month.)

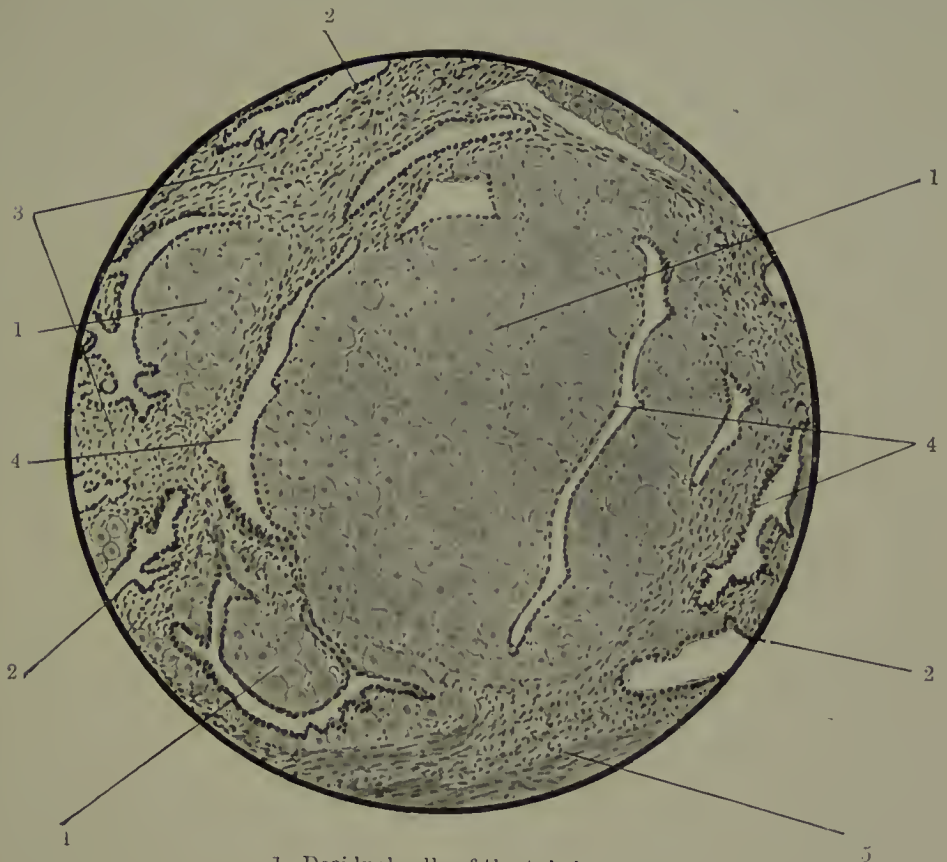


1. Chorionic villi with double epithelial covering.
2. Partially isolated syncytial off-shoots.
3. Langhans' layer of cells.
4. Blood-clot between the chorionic villi.
5. Muscular tissue of the tube wall.

(Haematoxylin-eosin stain.)

FIG. 42.

TUBAL DECIDUA. (Tubo-abdominal foetation at the eighth month ;
decidual development along the whole length of the tube.)



1. Decidual cells of the tubal mucosa.
2. Sequestered folds of the mucosa.
3. Normal stroma of the mucous membrane.
4. Much compressed superficial epithelial cells.
5. Muscular wall of the tube.

(Van Gieson's stain.)

at first hypertrophied, but with increasing development of the ovum a gradual thinning takes place which finally may lead to a complete atrophy of the muscular bundles. The muscular wall of the tube in interrupted pregnancy is often occupied by extensive hæmorrhagic collections, while the vessels are much increased in number and distended with blood. The peritoneal coat is sometimes occupied by decidual proliferations.

E.—DISEASES OF THE OVARIES.

(1) **Circulation Changes.**

The various conditions which are accompanied by congestion of the pelvic vessels (such as diseases of the heart, liver, and acute infectious diseases) also lead to hyperæmia of the ovarian vessels. Circulation changes also occur with new growths, impaction, and torsion of the pedicle.

As the result of hyperæmia a general serous infiltration into the ovarian stroma and connective tissue results (œdema of the ovary); in other cases, well marked hæmorrhage takes place into the ovary. Three chief varieties of the latter condition may be differentiated—follicular hæmorrhage, hæmorrhage into the corpora lutea, and interstitial hæmorrhage.

Follicular hæmorrhage or hæmatoma of a follicle, may sometimes attain the size of a fist; in some cases the hæmorrhage is confined to a single follicle, in others, many follicles are affected at the same time.

Similarly, hæmorrhage into a corpus luteum may lead to the formation of a tumour as large as a child's head. This may be differentiated from mere follicular hæmorrhage by the appearance of its capsule.

Hæmatoma of a follicle has generally only a very thin smooth wall, while the hæmatoma of a corpus luteum has

a thick folded wavy capsule, due to the characteristic formation of the lutein layers.

In rare cases hæmorrhage takes place into the stroma, the condition being termed ovarian apoplexy. Hæmorrhages of this nature are met with either in the form of small punctiform extravasations, or as large blood effusions involving the whole interstitial connective tissue. Twisting of an ovarian pedicle may also lead to hæmorrhagic infiltration and swelling of the ovary, which in some cases may reach the size of a small fist.

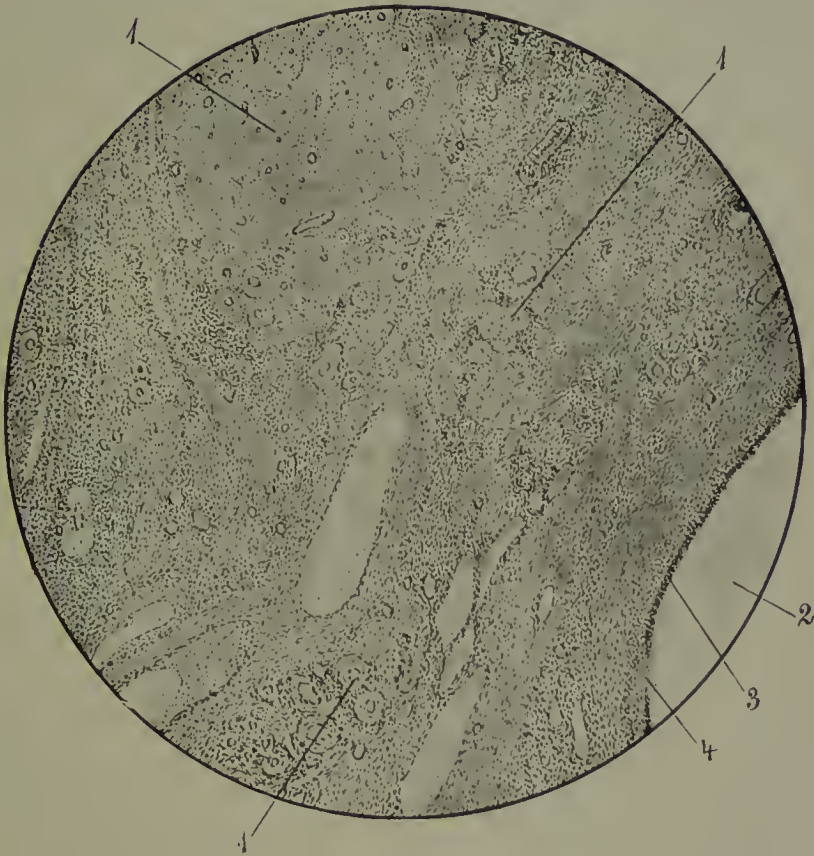
Microscopically, in cases of ovarian hyperæmia a well marked dilatation and increase of the vessels is apparent, which is especially noticeable in the region of the hilum. A considerable thickening of the vessel walls is also found, which later is accompanied with extensive hyaline degeneration. Hæmorrhages are also seen within the interstitial tissue (fig. 43), these may lead to hæmorrhagic necrosis of the whole ovary.

The contents of a hæmatoma of the follicle consist partly of fluid and partly of coagulated blood containing red blood corpuscles and their degeneration products, together with necrotic epithelial cells. The capsule of the tumour is lined internally by a single layer of cylindrical, cubical, or spindle-like cells; external to this comes the thin but very vascular tunica interna or propria; and lastly the dense fibrous tunica externa or fibrosa, consisting of dense connective tissue. In large hæmatomata the capsule only consists of extremely thin fibrous connective tissue.

In hæmatoma of the corpus luteum some cases are met with which are destitute of an epithelial lining, in others this is well marked; in the former the inner wall consists firstly of layers of fibrin, external to which is the thickened folded lutein cell layer. The lutein cells, however, are quite distinct, and maintain their normal characters. Outside this again comes the cellular con-

FIG. 43.

HYPERÆMIA, HÆMORRHAGE, AND HYALINE DEGENERATION OF
THE VESSELS OF THE OVARY.



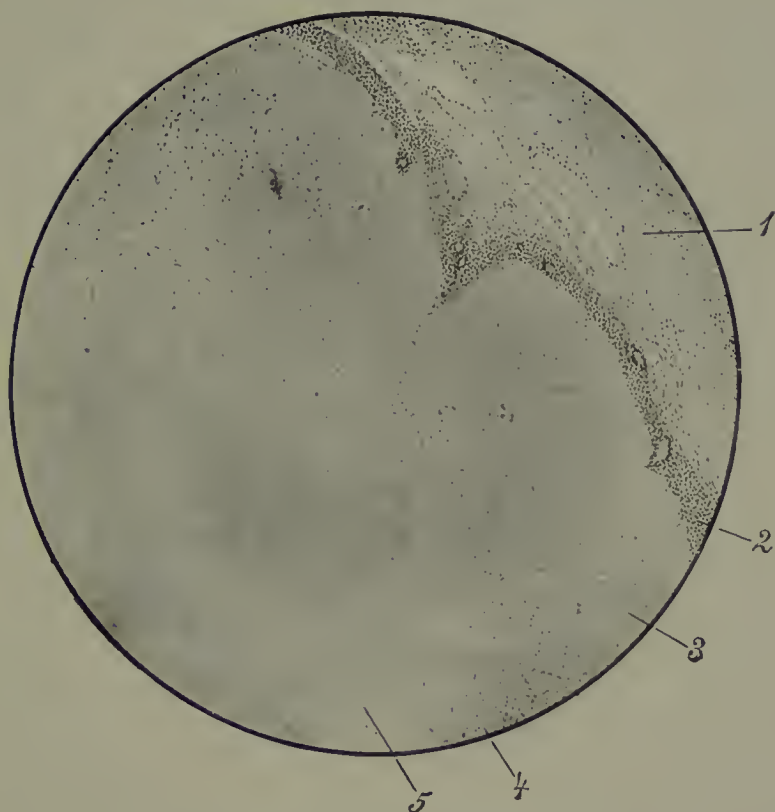
1. Arteries showing hyaline degeneration.
2. Follicle-hæmatoma.
3. Many-layered follicle epithelium.
4. Hæmorrhage into the wall of the follicle.

(Hæmatoxylin-eosin stain.)

FIG. 44.

HÆMATOMA OF THE CORPUS LUTEUM.

(Showing absence of epithelial lining.)



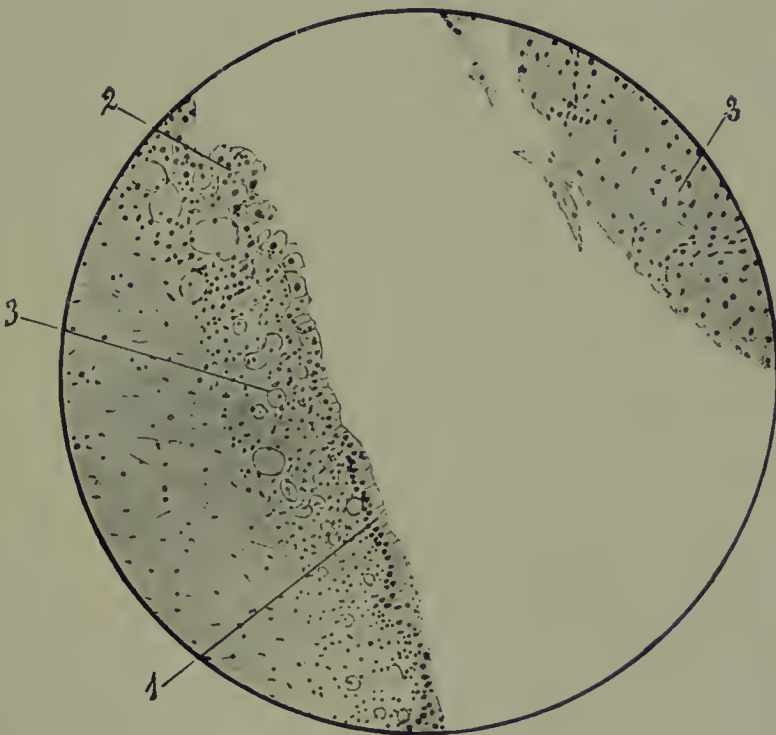
1. Connective tissue of the ovary containing dilated vessels.
2. Tunica externa or fibrosa.
3. Lutein-cell layer.
4. Fibrinous layer.
5. Blood-clot.

(Hæmatoxylin-eosin stain.)

FIG. 45.

HÆMATOMA OF THE CORPUS LUTEUM. Showing a definite epithelial lining.

(The contents have partly fallen out, on the right of the section the cyst wall is not covered with epithelium.)



1. Superficial cylindrical epithelium of cyst wall.
 2. Cubical and squamous epithelium.
 3. Lutein-cell layer with granular blood pigment and numerous vessels.
- (Hæmatoxylin-eosin stain.)

nective tissue of the tunica fibrosa, the outline of which follows the folds of the lutein cell layer (fig. 44).

In those hæmatomata of the corpus luteum which have a well marked epithelial lining, this consists of the cells of the lutein layer. These are single-layered and rest directly upon the cyst wall, and consist usually of cylindrical, cubical, or squamous cells (fig. 45).

The lutein cells remain well preserved for a long period, they often contain abundant blood pigment, and are surrounded by numerous engorged and dilated capillaries.

(2) Inflammation and Infective Granulomata.

(a) INFLAMMATION.

Inflammation of the ovary may be acute or chronic, and may either affect the interstitial connective tissue (oöphoritis interstitialis), or the whole ovarian structure (oöphoritis universalis).

Etiologically, inflammatory diseases of the ovary may be divided into two main groups, those that are due to gonorrhœal infection and those due to other causes. The latter comprise such infections as those due to streptococci and the bacterium coli communis. Micro-organisms may enter the ovary directly through the superficial epithelium, or by means of the blood-stream and lymphatic vessels.

(1) ACUTE OÖPHORITIS.—In the non-gonorrhœal variety of oöphoritis the ovary is at first free from adhesions; it is larger than normal, elastic to touch, and traversed by numerous injected vessels which stand out clearly amid the intensely œdematous parenchyma. Later, fibrinous adhesions and pseudo-membranes form on the peritoneal surface.

The gonorrhœal form generally commences as a peri-oöphoritis, and the ovary is enlarged and usually firmly

adherent to the tube. The vessels are increased in number and highly injected.

Microscopically in such cases, a well-marked small-celled infiltration of the interstitial connective tissue is seen following the track of the vessels (acute interstitial oöphoritis). According to the mode of infection it is most marked either in the neighbourhood of hilum or in the region of the peri-oöphoritic deposits; in the latter case the original germ epithelium is no longer visible (fig. 46).

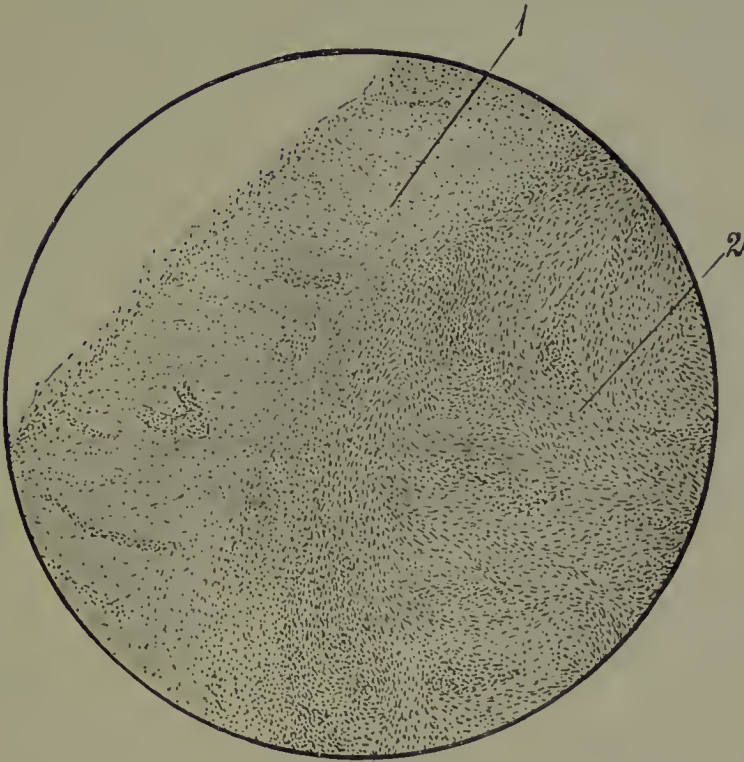
In time the inflammatory processes extend to all the follicles (oöphoritis acuta universalis), the vessels in their neighbourhood are injected, and hæmorrhages of various sizes are common. Whilst the ripening follicles are soon destroyed by the inflammatory processes, the epithelial lining of the mature follicles undergoes granular degeneration. Wandering leucocytes make their way into the follicles in large numbers destroying the epithelium, and finally suppuration occurs (fig. 47). The corpora lutea are affected by the inflammatory changes and become infiltrated with small round cells. It is quite unusual, however, to find micro-organisms in the inflamed tissues.

(2) CHRONIC OÖPHORITIS.—From their naked eye appearances two different varieties of chronic inflammation of the ovary can be recognised; in the first, the atrophied ovary appears to be completely converted into dense connective tissue, so that only a few, if any, follicles are met with. In the second, the ovary is enlarged and contains numerous cystic follicles which vary in size, the lining membrane of which is often very uneven and irregular. Cases coming under the first heading may be designated as oöphoritis chronica interstitialis, those in the second group as oöphoritis chronica universalis.

Microscopically, in *oöphoritis chronica interstitialis*, the

FIG. 46.

ACUTE INTERSTITIAL OÖPHORITIS. Secondary to peri-oöphoritis.

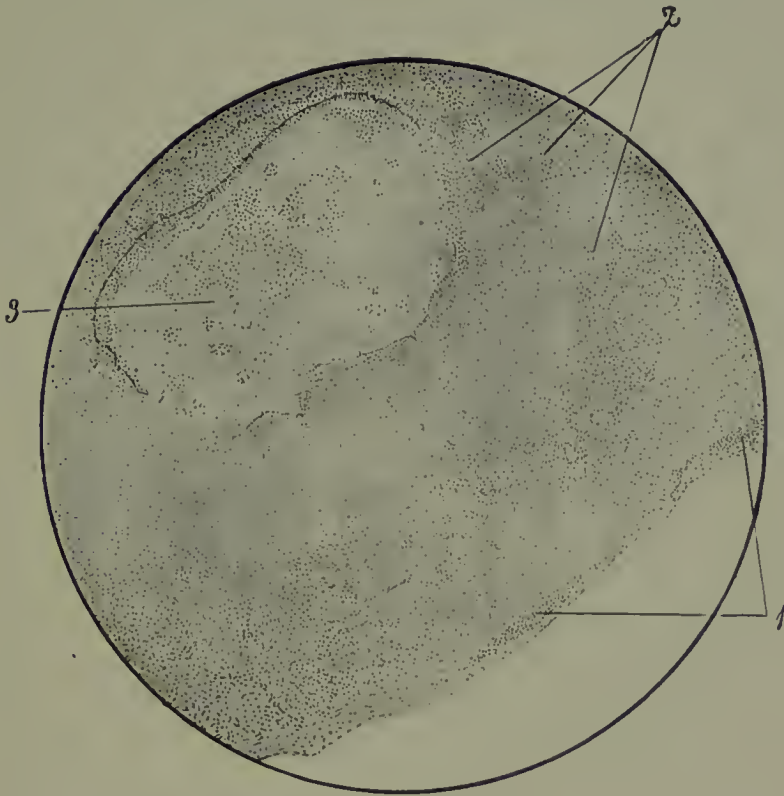


1. Wide peri-oöphoritic thickening, containing numerous newly-formed vessels and much small-celled infiltration.
2. Areas of small-celled infiltration in the outer covering of the ovary; all the follicles have disappeared.

(Hæmatoxylin-eosin stain.)

FIG. 47.

ACUTE OÖPHORITIS (*Oöphoritis acuta universalis*).

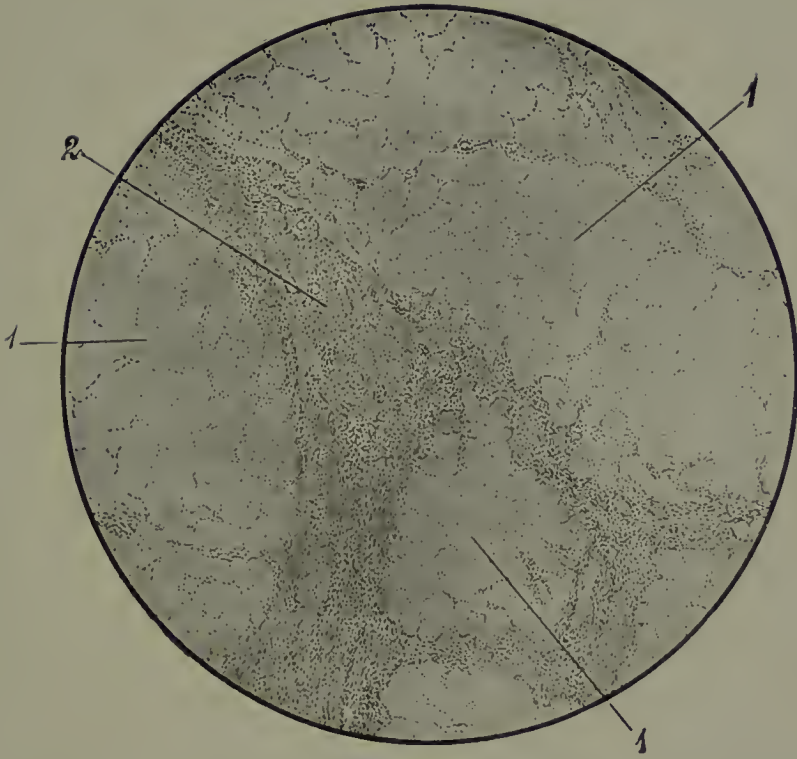


1. Small-celled infiltration within the tunica albuginea.
2. Small-celled infiltration of the stroma.
3. An inflamed follicle, in which the epithelium is partly wanting, and the vessels of which are engorged. The walls show much small-celled infiltration.

(Hæmatoxylin-eosin stain.)

FIG. 48.

CHRONIC INTERSTITIAL OÖPHORITIS.



1. Corpora albicantia, or fibrosa, resulting from hyaline degeneration of the vessels.
 2. Interstitial connective tissue, the vessels of which have undergone hyaline degeneration.
- (Hæmatoxylin-eosin stain.)

albuginea is much thickened and becomes converted into dense connective tissue with few nuclei, while here and there areas of hyaline degeneration are evident. The interstitial connective tissue is very rich in vessels, and small-celled infiltration areas are of frequent occurrence in their neighbourhood. The vessel walls are often extraordinarily thickened and frequently exhibit hyaline changes (fig. 48).

In some cases groups of vessels degenerate into large hyaline masses within the stroma, forming what are known as *corpora albicantia* or *corpora fibrosa*; these however may also arise from hyaline degeneration of the corpora lutea. The follicles themselves soon atrophy and disappear as the result of the compression of the inflamed interstitial tissue.

In *oöphoritis chronica universalis* there is often a considerable increase in the size of the ovary, due to the cystic degeneration of the follicles. The surface of the ovary may be quite smooth or may in other cases be nodular and uneven, owing to the presence of numerous rounded protuberances. On cutting into such an ovary many of the follicles undergoing cystic degeneration may be seen scattered throughout the stroma ("small cyst" degeneration).

Under the microscope well marked inflammatory changes are seen in the interstitial tissue, and hyaline degeneration of the vessel walls is often very extensive.

In the follicles, epithelial metamorphoses occur early, accompanied by an invasion of leucocytes. The epithelial cells show granular or hyaline degeneration, the ovum itself is destroyed by granular disintegration, while a complete disappearance of the epithelium of the follicle may occur, though this is very rare. The walls of the degenerated cystic follicles are often thickened as the result of the proliferation of the connective tissue. The primordial follicles are soon destroyed, and in the end the corpora lutea are comparatively few in number.

(3) ABSCESS OF THE OVARY.—Inflammation of the ovary sometimes ends in the formation of an abscess, which according to its position may be differentiated into three varieties, viz., the *interstitial abscess*, *abscess of the follicle*, and *abscess of the corpus luteum*, the last being the most commonly met with. An abscess of the ovary varies greatly in size, it may be very minute, but in some cases reaches the size of a fist or even a man's head.

Abscess of the corpus luteum has a particularly characteristic appearance. The inner wall is lined with papillary proliferations varying greatly in size which project from the wavy yellow lutein layers. The proliferations in their fresh state give a velvety appearance to the inner wall of the abscess cavity.

Abscess of the follicle in its early stages generally has a smooth lining membrane, but later this may become uneven and fasciculated.

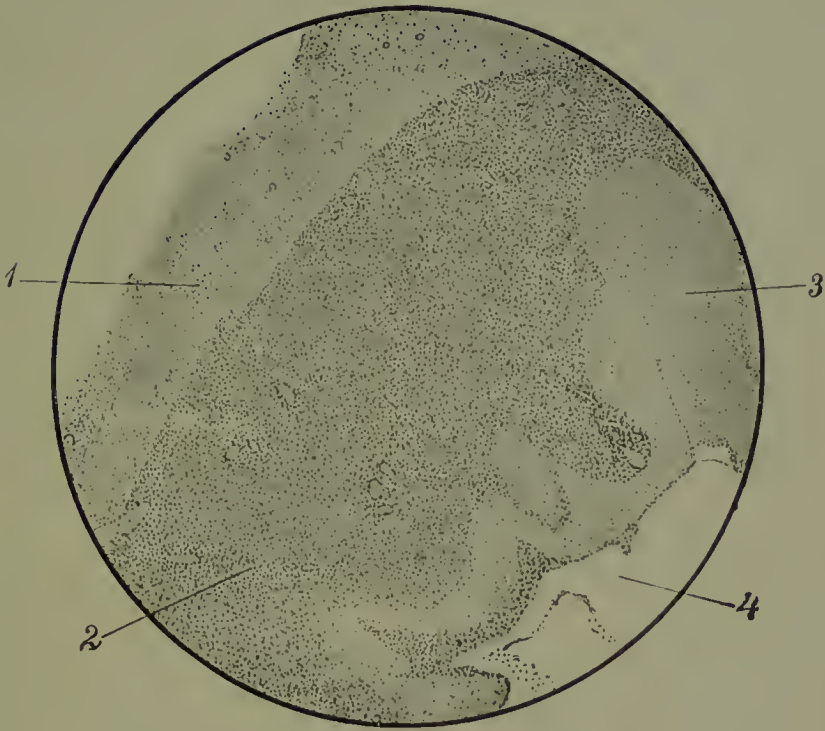
The *interstitial abscesses* are not usually sharply defined from the surrounding tissues. They originate from gradual suppuration of the ovarian stroma, which in the end involves the follicles and corpora lutea. The foci of suppuration may occur either in a single group, or there may be many such areas scattered through the stroma. By the communication of an ovarian abscess with a *sactosalpinx purulenta* (*pyosalpinx*) a so-called tubo-ovarian abscess is formed.

Microscopically the structure of an *abscess of the corpus luteum* is very characteristic; its inner wall is lined with a layer of exceedingly vascular granulation tissue arranged in small convex papillary swellings; these being apparently derived from the original lutein cell layer (fig. 49).

It very often happens in spite of the large accumulation of round cells amid the leucocytes, that some larger cells with pale nuclei can be distinguished, which from

FIG. 49.

COMMENCING ABSCESS OF THE CORPUS LUTEUM.



1. Tunica albuginea, which is very vascular and infiltrated with small cells.
2. Lutein-cell layer, also much infiltrated with small cells.
3. Fibrinous coagulum in one of the recesses of the lutein-cell layer.
4. Lumen of the corpus luteum, containing pus.

(Hæmatoxylin-eosin stain.)

their shape are evidently the remains of the original lutein cell layer. The wide areas of small-celled infiltration become transformed into dense connective tissue and may eventually undergo hyaline degeneration. The surrounding connective tissue is very vascular, and everywhere occupied by accumulations of small round cells.

Abscess of the follicle generally has a more uniform lining of granulation tissue; the original epithelium soon disappears, and a distinction between the different layers of the abscess wall cannot be made out owing to the intensity of the small round-celled infiltration. The surrounding stroma is also similarly infiltrated with small cells and has a rich vascular supply.

Interstitial abscesses arise by the gradual fusion of numerous areas of suppuration which occupy the stroma. At first the abscess wall is ill defined, but later a dense capsule of connective tissue is formed apparently developed from the tunica albuginea; this latter structure however shows great powers of resistance to the inflammatory processes. Finally, in chronic abscess it may be almost impossible to recognise any of the component parts of the original ovarian connective tissue. Micro-organisms may sometimes be found in the pus of an ovarian abscess, but they rarely occur in the abscess wall or the surrounding connective tissue.

(b) INFECTIVE GRANULOMATA.

Among the infective granulomata of the ovary, syphilis, actinomycosis, leprosy, and tuberculosis, have been observed, the last being the most important. It is questionable whether primary tuberculosis of the ovary occurs. Up to the present time it has not been observed with sufficient certainty to warrant a separate description. Tubercle of the ovary probably in every case is secondary to tubercle of the Fallopian tube and peritoneum.

Tubercle of the ovary occurs in two different forms, either as a tuberculous peri-oöphoritis or a true tuberculosis of the ovary; the former may be either disseminated or diffuse.

With disseminated tuberculous peri-oöphoritis numerous small isolated tuberculous nodules are seen scattered either over a portion or the whole surface of the ovary. In diffuse tuberculous peri-oöphoritis numerous thick confluent masses are seen occupying the surface of the ovary. These thickenings are made up of smaller tuberculous nodules.

True tuberculosis of the ovary is usually met with in the miliary form, but cheesy deposits and abscesses are also found; the first is most frequent, the two latter not uncommonly occur together. The cheesy areas in the ovary may vary from the size of a pin's head to that of a hazel-nut, while an abscess may attain the size of a child's head. Macroscopically, the miliary variety cannot be recognised with certainty, but may be suspected by the accompanying tuberculous peri-oöphoritis.

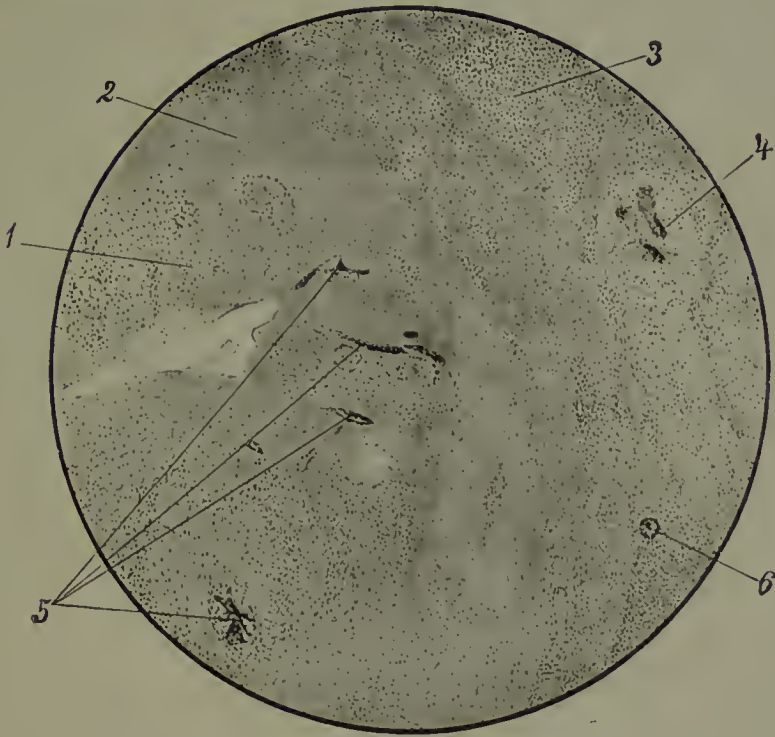
Microscopically, in tuberculous peri-oöphoritis, either small isolated tuberculous nodules with epithelioid cells and giant cells are met with, or extensive tuberculous deposits occur containing characteristic tuberculous nodules and numerous isolated giant cells. Here and there amid the thickened patches, commencing caseous changes are not uncommon.

In miliary tuberculosis of the ovary the stress of the disease falls upon the interstitial connective tissue. Depending on the site of infection, isolated granulation cells and giant cells are met with in the region of the hilum or on the surface epithelium. Later in the course of the disease typical tuberculous nodules occur, these are frequently surrounded by a dense stratum of connective tissue which may be seen to send solitary off-shoots into the tuberculous nodules.

FIG. 50.

MILIARY TUBERCULOSIS OF THE OVARY.

Showing tubercle of a corpus luteum and interstitial connective tissue.)



1. Lutein-cell layer with tuberculous nodules and isolated giant-cells.
2. Tunica externa.
3. Small-celled infiltration.
4. Tuberculous nodules in the interstitial connective tissue.
5. Isolated giant-cells in the lutein-cell layer.
6. Normal follicle.

(Hæmatoxylin-eosin stain.)

Whether the disease arises from the hilum or from the surface of the ovary, it invariably leads to the gradual formation of granulatinous cells, migratory cells, and giant cells, within the ovarian tissues.

Although miliary tuberculosis of the follicle has not been hitherto observed, it may certainly affect the corpus luteum. In this case a direct infection of the inner surface of the corpus luteum apparently takes place from the pus of a tuberculous tube, and leads to an extensive formation of tuberculous nodules within the lutein layers. The nodules are extraordinarily rich in giant cells, which exhibit many fine off-shoots (fig. 50).

From the corpus luteum the disease spreads into the connective tissue stroma, in which numerous tuberculous nodules are met with. These are also seen in the immediate neighbourhood of the follicles, but the follicles themselves rarely show any tuberculous changes. In the caseous form, rounded or ribbon-like areas of tubercle are seen scattered throughout the whole ovary, while in their immediate neighbourhood numerous areas of round-celled infiltration are as a rule met with. Giant cells are rare. In tuberculous abscess, the inner wall is seen to be lined with friable cheesy masses, the wall of the abscess itself consisting of granulation tissue in which typical tuberculous nodules and giant cells are embedded. Such abscesses may or may not contain tubercle bacilli, these being mostly found within the giant cells or in the caseous areas of degeneration. Tubercle affecting an ovarian tumour is usually due to secondary infection from the peritoneum. The cyst wall is first attacked, then the deeper parts, and finally the whole contents of the cyst are transformed into a purulent caseous mass.

(3) New Growths.

(a) INNOCENT NEW GROWTHS.

(1) SIMPLE CYSTS.—The simple cysts of the ovary (inflammatory, parasitic, and retention cysts) originate in

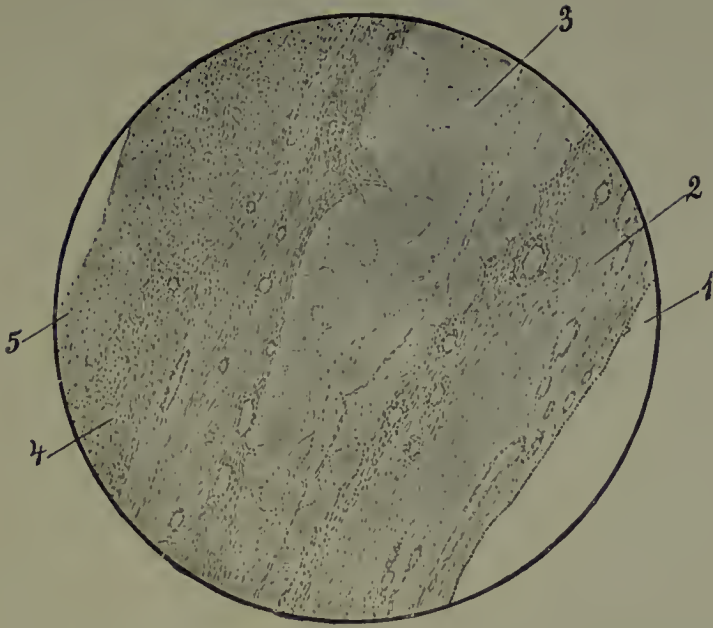
by far the greater number of cases as the result of inflammatory changes; they may also arise from pre-existing cavities, such as the follicles, or the corpora lutea. Two chief varieties may be differentiated: (i.) the *follicle cysts*, and (ii.) *the cysts of the corpora lutea*. Should a communication form between one of these cysts and the Fallopian tube a so-called tubo-ovarian cyst is formed.

(a) *The Follicle Cysts*.—The size of follicle cysts varies between that of a hazel-nut and a man's head, while their shape is usually rounded or oval. As long as they do not exceed a certain size such cysts may be multiple, but as a rule one cyst gradually grows larger to the detriment of the others, so that large cysts almost always occur singly.

The thickness of the cyst wall depends upon its size. By increasing distension the wall may become as thin as a sheet of paper. The inner surface is nearly always perfectly smooth, and may have a fascia-like appearance. In very rare cases isolated papillary proliferations may occur on the lining membrane. These cysts usually contain a pale watery, or serous fluid.

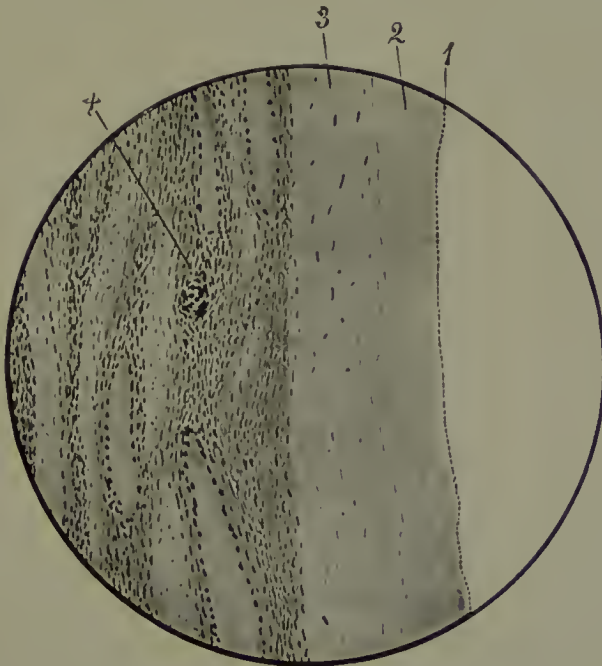
Microscopically the cysts are always lined with a single layer of epithelium, which as a rule consists of low cylindrical, cubical, or even spindle-shaped cells. In places these cells exhibit fatty degeneration. The cyst wall itself consists of two layers, which correspond to the tunica propria or interna, and the tunica fibrosa or externa. In small cysts the inner layer consists of a loose vascular cellular stratum, while the outer is dense and contains but few cell elements (fig. 51). In larger cysts, the inner layer is often extremely poor both in cells and vessels, while the outer may contain rather more cells (fig. 52). As the cyst increases in size the two layers become more and more difficult to differentiate, the walls finally consisting only of dense fibrous tissue. The

FIG. 51.
SMALL FOLLICLE CYST.



- | | |
|--|------------------------------|
| 1. Cubical epithelium lining the cyst. | 4. Connective tissue stroma. |
| 2. Vascular tunica externa. | 5. Tunica albuginea. |
| 3. Corpus albicans. | |
- (Hæmatoxylin-eosin stain.)

FIG. 52.
LARGE FOLLICLE CYST.



- | | |
|--|---|
| 1. Low cubical epithelium lining the inner wall of the cyst. | 3. Tunica externa. |
| 2. Tunica interna, poor in cell elements. | 4. Connective tissue stroma of the ovary. |
- (Hæmatoxylin-eosin stain.)

various component parts of the original ovarian tissue can no longer be recognised.

In very rare cases small papillary proliferations occur on the inner wall of these follicle cysts; they originate from an increase of the connective tissue in the cyst wall, which pushes the lining epithelium before it towards the cyst cavity. If these papillary proliferations increase in size, as they may do, they are seen to consist of loose reticulated connective tissue containing only few cell elements. They are always covered by a single layer of epithelium consisting of low cylindrical or cubical cells, and sometimes by ciliated epithelium (fig. 53).

(b) *Cysts of the Corpora Lutea*.—Corpus luteum cysts may vary in size from a cherry-stone to a man's head; they usually occur at one or other pole of the ovary. The cyst wall is very characteristic in appearance, and is always of great thickness even in large cysts.

Macroscopically two definite layers can always be easily made out in the cyst wall. The inner is a wavy folded yellowish or brownish layer; this gives an uneven and furrowed appearance to the lining of the cyst and arises from the lutein cells. The outer layer is always very dense, and is developed from the tunica fibrosa. These cysts usually contain clear serous fluid which is sometimes mixed with blood.

Microscopically two varieties of corpus luteum cysts may be differentiated, viz., those destitute of an epithelial lining, and those in which this is well marked. In the first variety the lining membrane usually consists of a mere fibrinous layer or loose connective tissue extending in amid the folds of the lutein cell layer, which is external to it. The lutein cell layer may be well preserved for long periods, and is composed of the characteristic lutein cells, among which numerous blood vessels are seen. Sometimes the cyst wall undergoes extensive hyaline degeneration.

Epithelial-bearing corpus luteum cysts possess (instead of a fibrinous or connective tissue layer) a lining which is seen to consist of a single layer of cells having great diversity of shape (fig. 54). The cells are usually cylindrical, but cubical or even squamous cells occur; in large cysts the cubical type of cell is usually found. The epithelial cells are immediately superficial to the lutein cell layer. The latter always maintains its characteristic wavy or folded appearance, although the lutein cells may gradually disappear. The lutein cells after a time may be replaced by connective tissue cells, between which numerous vessels are often met with (fig. 55).

(2) ADENOMATOUS CYSTS.—The adenomatous cysts of the ovary are epithelial new growths, which arise from its superficial epithelium ("Müller's epithelium") not apparently from the normal germ epithelium.

Cystic adenomata of the ovary may be divided into two groups, according either to the nature of their contents or to the nature of the growth. To the first series belong the pseudo-mucinous adenomatous cysts and the serous adenomatous cysts. Under the second heading are the proliferating glandular cysts (cystadenoma proliferum glandulare, s. evertens) and the papillary proliferating cysts (cystadenoma proliferum papillare, s. invertens).

(a) *Pseudo-mucinous Adenomatous Cysts*.—(i.) *Glandular pseudo-mucinous cysts*. This variety is by far the most common of all ovarian tumours. Such cysts may be either unilateral or bilateral; their size may often considerably surpass that of a man's head, and they are commonly rounded or oval in shape. They usually have a broad pedicle, but they may develop between the layers of the broad ligament. Unilocular cysts generally have a uniform smooth covering, while multilocular cysts often possess lobes and bosses owing to the main tumour being composed of innumerable other cysts.

FIG. 53.

FIBRO-PAPILLARY OVARIAN CYST.



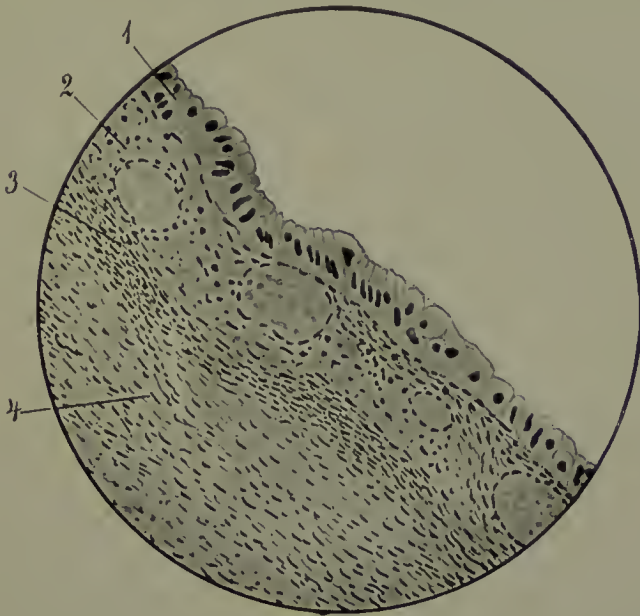
1. A large connective tissue papilla springing
from the inner wall of the cyst.
2. A smaller papilla.

3. Tunica interna.
4. Tunica externa.
5. Tunica albuginea.

(Hæmatoxylin-eosin stain.)

FIG. 54.

CYST OF THE CORPUS LUTEUM, LINED BY EPITHELIUM.



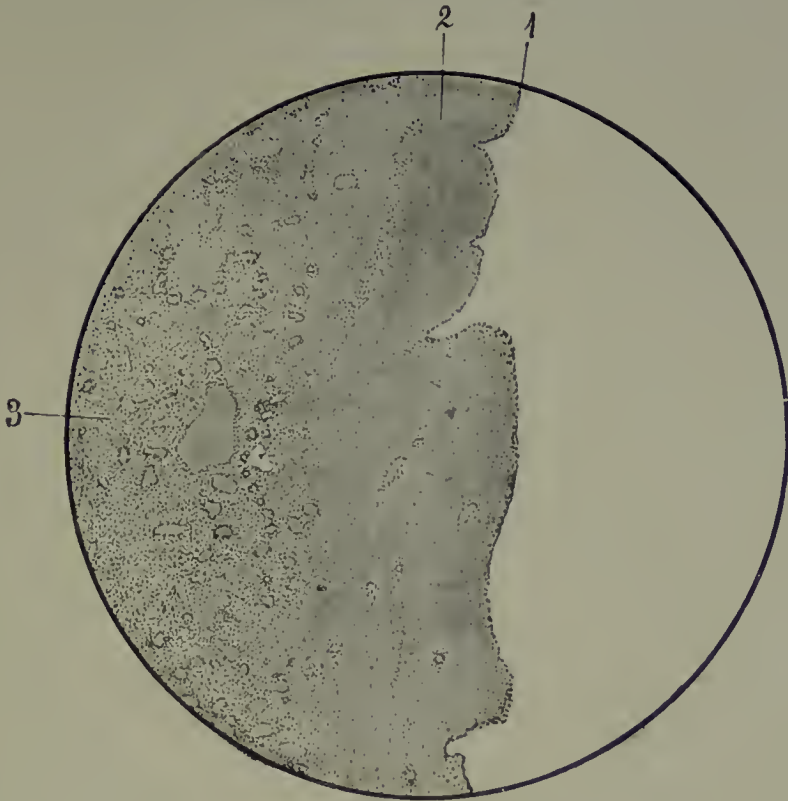
1. Polymorphous epithelial lining.
2. Lutein-cell layer.

3. Tunica externa.
4. Connective tissue stroma of the ovary.

(Hæmatoxylin-eosin stain.)

FIG. 55.

CYST OF CORPUS LUTEUM, LINED BY DEFINITE EPITHELIUM.



1. Cubical epithelium of the lining membrane.

2. Lutein-cell layer.

3. Connective tissue stroma with numerous vessels.

(Hæmatoxylin-eosin stain.)

FIG. 56.

GLANDULAR PSEUDO-MUCINOUS CYST.



1. Glandular spaces lined with tall cylindrical epithelium.

2. Interstitial connective tissue.

(Hæmatoxylin-eosin stain.)

As a rule however in tumours of this sort a main cyst with numerous daughter or accessory cysts can be differentiated. The main cyst arises from a union of several smaller cysts; this is often clearly shown by the septa occurring on its inner surface. The thickness of the cyst wall varies with the size of the tumour, the larger the cyst the thinner are its walls; these as a rule are rich in vessels.

It sometimes happens that the tumour is made up of a large number of thin pedunculated cysts of various sizes, and to the naked eye looking somewhat like a bunch of grapes (grape or cluster-forming cysts).

The lining membrane of a pseudo-mucinous cyst is either smooth and velvety and yellowish in colour, or it is irregular and traversed by different ledges and septa. In some cases the walls are bulged inwards by neighbouring cysts. The cysts contain either a characteristic tenacious viscid material, or thin honey-like sticky fluid. The fluid varies greatly in colour, and may be whitish-yellow, reddish-brown, or dark green. The most characteristic constituent of the fluid is pseudo-mucin (the chief secretion of the specific epithelium); this has a ropy gelatinous transparent consistency.

Under the microscope the ovarian fluid contains degenerate epithelial cells, fat globules, cholesterine crystals, as well as blood corpuscles and their products of degeneration.

The walls of unilocular cysts consist of three layers—an inner lining of epithelium, a middle layer of fibrous connective tissue, and an outer covering of normal germ epithelium of the ovary. In multilocular cysts the middle layer often contains numerous glandular epithelial depressions and cyst-like spaces (fig. 56).

The epithelial lining of such cysts often has a striking resemblance to that of the glands of the cervix uteri. It consists of tall cylindrical epithelium, with large

rounded nuclei (situated at the base of the cells) and bright granular protoplasm. The epithelium however may become flattened by increasing pressure from within.

The cell protoplasm consists of two layers—a basal granular albuminous layer and a clear central homogeneous pseudo-mucinous layer. Goblet cells are common. The epithelial cells may undergo a fatty or myxomatous change which causes them to assume a club-shaped appearance. The epithelium is always single-layered, but may sometimes form papillary outgrowths into the lumen of the cyst (fig. 57).

In large cysts three layers can usually be distinguished in the wall, the outer being dense connective tissue, the middle consisting of loose vascular tissue, while the inner is made up of innumerable cells. In small cysts the walls contain numerous gland-like spaces lined with characteristic epithelium; these arise from epithelial ingrowths which become cut off and frequently join one with another, so giving rise to the formation of new cyst cavities. Remnants of former cyst walls can often be recognised projecting into the interior of such cysts.

The outer layer of the cyst wall consists of the normal superficial germ epithelium the cells of which have a low cylindrical or cubical shape. As the result of pressure the epithelium disappears, and adhesion of the cyst wall to neighbouring organs readily occurs.

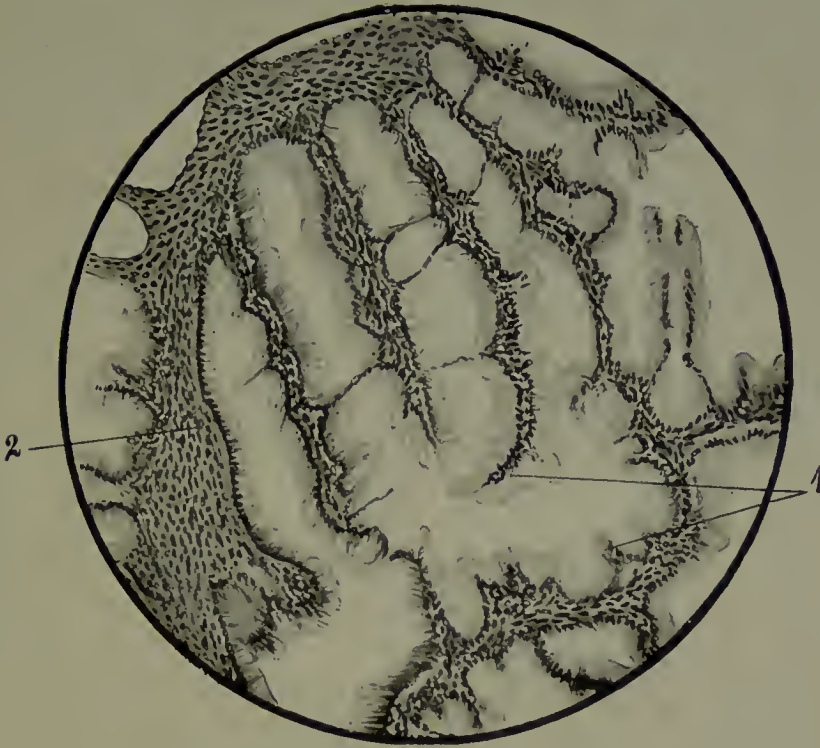
The cyst walls may undergo various secondary changes, such as hæmorrhagic infarction, fatty and myxomatous degeneration. Malignant changes in the form of sarcomatous degeneration of the wall, and carcinomatous degeneration of the epithelium, are also met with.

Rupture of a pseudo-mucinous cyst may lead to the formation of gelatinous deposits upon the peritoneum (pseudo-myxoma peritonei). Glandular pseudo-mucinous cysts may occur in connection with embryomata.

(ii.) *Papillary Pseudo-mucinous Cysts.* — Papillary

FIG. 57.

GLANDULAR PSEUDO-MUCINOUS CYST.



1. Ledge-like papillary outgrowth within the gland-like acini.
2. Interstitial connective tissue.

(Hæmatoxylin-eosin stain.)

FIG. 58.

SEROUS PAPILLARY CYST.



1. Papillary growths, covered with cylindrical epithelium.
2. Interstitial connective tissue.

(Hæmatoxylin-eosin stain.)

pseudo-mucinous cysts are not nearly so common as the variety just described; they are usually pedunculated, and may be unilateral or bilateral. They sometimes grow between the folds of the broad ligament. They do not exist in such variety as the pseudo-mucinous cysts, nor are they usually so large. In multilocular papillary cysts the component cysts are as a rule more uniform in size, so that these tumours are made up of many rather than one main cyst.

The most characteristic feature of these cysts is the occurrence of papillary growths of various sizes which project into the main cyst cavity. Rarely these growths may occur on the outer surface of the cyst wall. In most cases the papillæ are long and slender, with a delicate stroma. Small cysts may be completely filled by such growths. In large cysts they only occur here and there in isolated patches upon the lining membrane. The papillæ are soft in consistency, reddish-yellow in colour, and more or less resemble warts, but as a result of œdematous swelling they may eventually become globular in shape.

Microscopically, the papillæ are covered with tall cylindrical epithelium similar to that of the glandular cysts. Unlike the epithelium of serous papillary cysts, the papillæ are never covered with ciliated epithelium. Their stroma consists entirely of delicate fibrillary connective tissue, which here and there is rich in vessels; sometimes the stroma is very œdematous, or shows signs of mucoid degeneration.

The papillæ arise by a vigorous proliferation of the lining epithelium, which grows so rapidly that there is no longer any room for it on its original connective tissue bed, and it thus becomes crowded forward in a papillary manner into the lumen of the cyst. The stroma proliferates into the papillæ secondarily, in most cases accompanied by capillary loops of blood-vessels.

(b.)—SEROUS CYSTS.

(i.) *Glandular Serous Cysts*.—The serous glandular cysts are comparatively rare, they are mostly unilocular and are seldom as large as the pseudo-mucinous cystomata, though in other respects they are very similar. They contain clear serous fluid which is rich in albumin but destitute of pseudo-mucin.

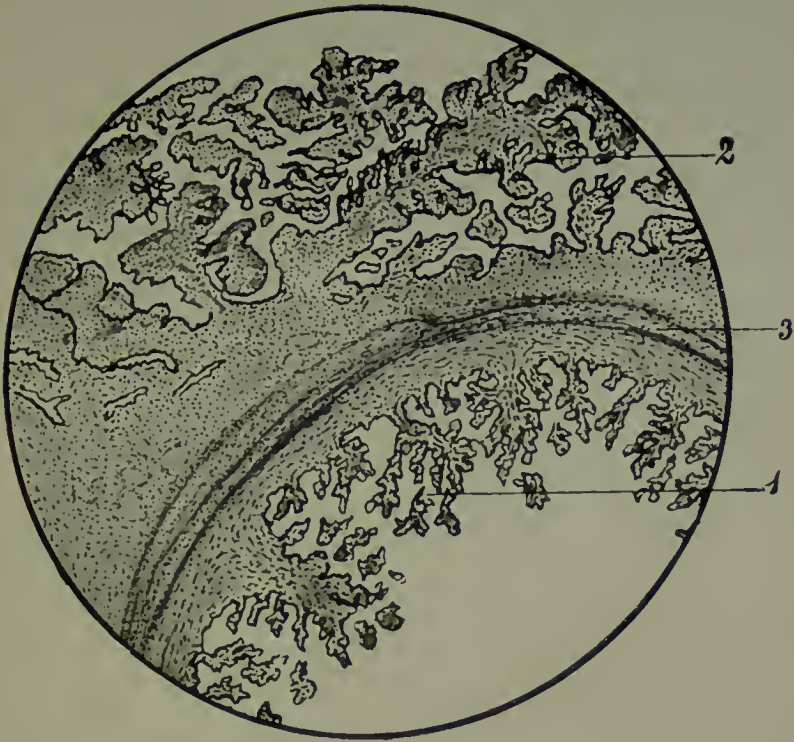
Microscopically, such cysts are lined with a single layer of tall cylindrical cells having an oblong centrally-placed nucleus and distinct cilia. Their wall consists of loose fibrillated connective tissue, and is beset with numerous gland-like spaces which are lined with ciliated epithelium. They vary very much in the amount of their vascular supply.

(ii.) *Papillary Serous Cysts*.—Papillary serous cysts, also called ciliated papillary cysts, are comparatively common. They are very frequently bilateral, and sometimes grow between the layers of the broad ligament. The tumours are more often unilocular than multilocular. In multilocular cysts the small cyst cavities are often completely filled with papillary growths, while in the larger cysts these occur in isolated groups on the smooth lining membrane. The papillæ may either consist of small low warty outgrowths, or they may be slender villous and branched in all directions. They have a yellowish-red appearance, and are often extremely soft and friable. The stroma in some cases is somewhat firm, but owing to œdematous swelling or myxomatous degeneration the papillæ become vesicular and may closely resemble a hydatidiform mole.

The papillary growths may develop in great numbers exclusively on the surface of the tumour, either unbranched and characterised by a dense stroma, or else as branching papillomata. The branched papillomata are either primary or secondary; in the latter case they originate from papillary growths lining the cyst which

FIG. 59.

SEROUS PAPILLARY CYST. Showing both varieties of Papillomata.

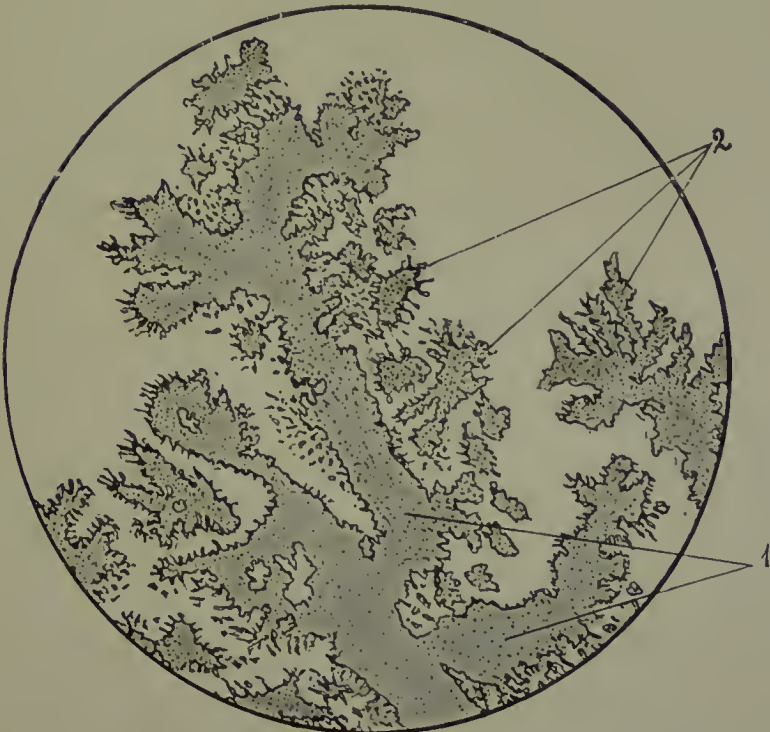


1. Intra-cystic papillary growths.
2. Extra-cystic papillary growths (surface papillomata) with dense stroma.
3. Cyst wall.

(Hæmatoxylin-eosin stain.)

FIG. 60.

SEROUS PAPILLARY CYST.



1. Papillæ, showing abundant stroma.
2. Secondary papillæ, much branched.

(Hæmatoxylin-eosin stain.)

break through the cyst wall and then continue to grow on the surface.

These cysts always contain pure serous fluid, but from admixture of degenerated epithelium or blood, it may be turbid, yellowish-green, or resemble pea-soup.

Surface papillomata are usually associated with ascites, and frequently form metastases upon the peritoneum.

Microscopically both the smooth lining membrane and the papillary outgrowths are usually covered with tall cylindrical epithelium. The cells are often ciliated, and possess oblong centrally placed nuclei. In places epithelial invaginations and constrictions occur giving rise to gland-like spaces, the epithelium of which always consists of a single layer (fig. 58).

The stroma of the papillæ consists of a variable amount of connective tissue framework not very rich in vessels. It is characteristic of the pure surface papillomata that their connective tissue framework is much more abundant and much denser than that of the papillæ developed from the interior of the cyst (fig. 59).

The papillæ result from an active proliferation of the epithelial cells lining the cyst. They at first occur as tuft-like elevations, into which the connective tissue stroma and the vessels grow secondarily. This process is repeated indefinitely, till at length a most complicated papillary tumour formation results. According to the amount of connective tissue stroma the papillæ may either be low and club-like in form, or they may have a tall slender appearance (fig. 60).

Secondary changes may frequently be seen in the stroma owing to disturbances of nutrition. Myxomatous degeneration is most commonly observed. This causes a club-like thickening of the papillæ and gives them a vitreous or transparent appearance. As a rule myxomatous degeneration of the epithelial cells occurs at the same time, so that these also appear swollen, vesicular,

and club-like. This is particularly noticeable at the free extremities of the cells, the base appearing thinned out and almost pedunculated (fig. 61). In this way the cells may be gradually destroyed.

Chalky deposits are not uncommon in the connective tissue stroma in the form of concentrically-arranged psammomata, but they must not necessarily be put down to retrograde changes as they are found in quite young papillæ. These deposits sometimes occur in such extraordinary numbers that they impart a gritty sensation to the cut surface of the tumour.

Among malignant changes affecting papillary cysts, carcinomatous degeneration is the most frequent.

(3) THE EMBRYOMATA (DERMOIDS AND TERATOMATA).

Ovarian embryomata consist of two groups—the simple cystic embryomata (dermoids), and the solid embryomata (teratomata). All ovarian embryomata are products of one of the three layers of the original germ epithelium; this renders the assumption that they arise from an included ovum quite superfluous.

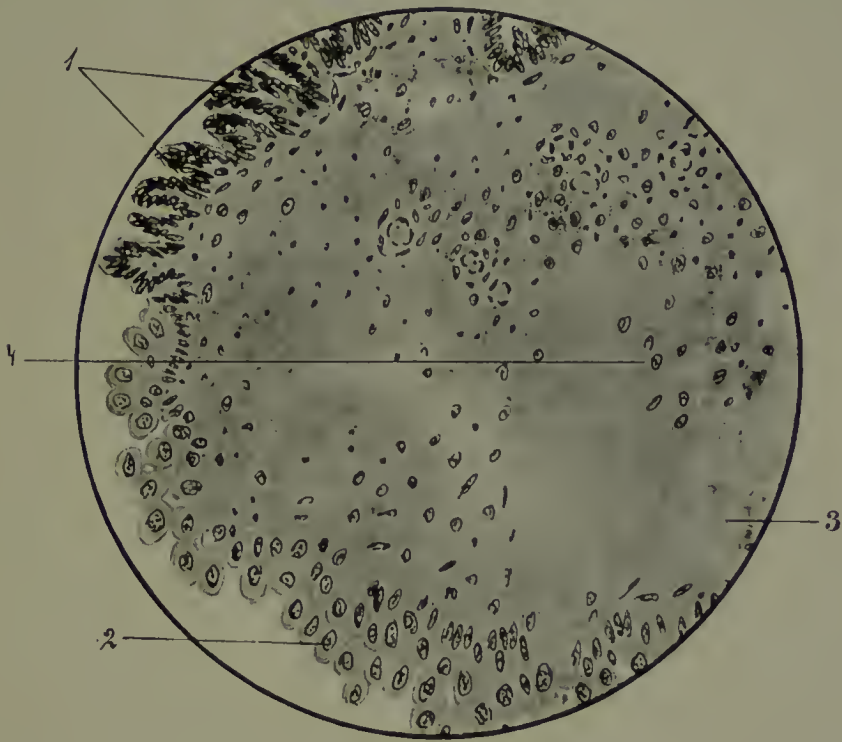
(a) *Cystic Ovarian Embryomata (Dermoids).*—The size of such tumours varies from that of a walnut to that of a man's head. They are mostly rounded or oval in shape, and have a smooth surface. Their walls vary much in thickness, and nearly always contain remains of ovarian tissue which is either normal in appearance or which exhibits cystic degenerative changes. Dermoids always contain hair, and a thick fluid or semi-solid fatty material which is yellowish in colour.

Microscopically the contents consist of degenerate epithelial cells, fat globules, granular detritus, and cholesteroline crystals.

Ovarian embryomata are usually single, but they may be multiple. These multiple growths must not be mis-

FIG. 61.

SEROUS PAPILLARY CYST UNDERGOING MYXOMATOUS CHANGES.

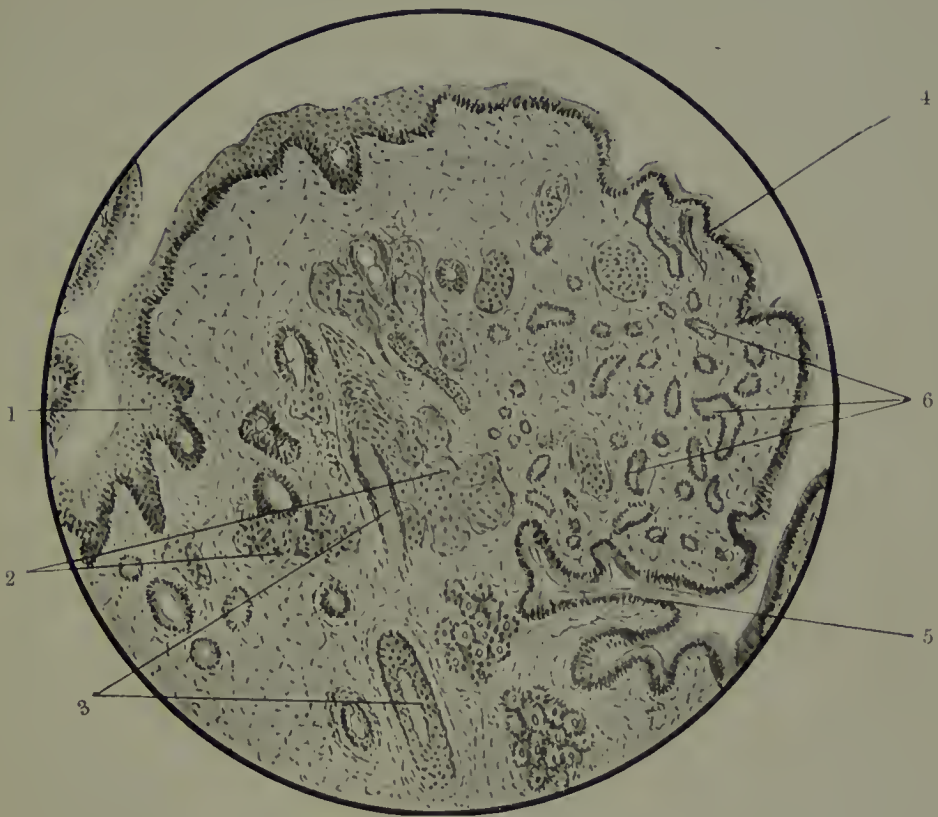


1. Papillae with normal cylindrical epithelium.
2. Epithelium undergoing myxomatous degeneration becoming clubbed and vesicular in appearance.
3. Stroma, showing homogeneous myxomatous degeneration.
4. Degenerate connective tissue cells.

(Hæmatoxylin-eosin stain.)

FIG. 62.

SOLID OVARIAN EMBRYOMA (WILMS).



1. Squamous epithelium of the cutis.
2. Sebaceous glands.
3. Hair follicle.
4. Ciliated epithelium of the endoderm.
5. Gland tube with ciliated epithelium.
6. Smaller gland-lumina.

taken for a combination of an embryoma and a cyst, which presents a similar appearance; in the latter case, the embryoma grows into the cyst secondarily.

Villous outgrowths are frequently seen upon the inner wall of cystic ovarian embryomata. These are covered with skin and hair, while the remainder of the lining membrane is smooth. Bone and teeth occur frequently in the neighbourhood of these outgrowths.

Microscopic examination shows that while the greater part of the cyst wall consists of a loose layer of granulation tissue, in the region of the villous outgrowths all three layers of germ epithelium are represented.

Formations from the ectoderm predominate, such as skin, sebaceous glands, sweat glands, hair, epidermal bone, brain matter, and optic rudiments. The mesoderm is represented by connective tissue, muscular tissue, fat, true bone and cartilage; while from the entoderm, mucous cysts, cysts lined with ciliated epithelium, mucous glands, and glands resembling those of the intestine and thyroid, are found.

(b) *Solid Ovarian Embryomata (Teratomata)*. — Solid ovarian embryomata are very rare, but they sometimes reach the size of a man's head. Their shape is usually uneven and nodular, and their surface smooth.

On section such tumours are beset with numerous smaller cysts. The main tumour mass is solid and presents the most extraordinary diversity in appearance, colour, and consistency. The cysts are partly lined with epidermal structures and partly with mucous membrane, and contain sebaceous material mixed with hair, or a mucoid fluid.

Microscopically they contain derivatives of all three germinal layers, but in contradistinction to the cystic embryomata, the contents show no tendency to any regular formation, but occur in hopeless confusion, and without any limit to their growth (fig. 62).

Carcinomatous or sarcomatous changes may occur in ovarian embryomata.

(4) CONNECTIVE TISSUE NEW GROWTHS.—The innocent connective tissue tumours of the ovary are comparatively rare. Fibromata are most frequently met with, myofibromata and myomata are less common. The remaining tumours belonging to this class (myxomata, osteomata, enchondromata, angiomas, and lymphangiomas) are so rare that they are hardly worth special consideration.

(i.) *Fibromata*.—Two varieties of ovarian fibromata may be recognised—the *surface* fibroma and the *diffuse* or *pure* fibroma. The latter is very rare.

(a) The surface fibromata occur in the form of small mushroom-like or polypoid growths springing from the tunica albuginea. They are not usually larger than a pea or a hazel-nut, and often have a broad pedicle. They are very hard. On section they consist chiefly of a dense network of thick white fibrous bundles. Their surface may be either quite smooth, or grooved and furrowed.

Microscopically these tumours consist of the dense fibrous or reticulated connective tissue of the albuginea, and contain but few vessels and cell elements. The surface is clothed with germ epithelium which is most clearly seen in the depths of the furrows in the region of the pedicle. Chalky formations are sometimes found in these tumours (fig. 63).

In rare cases these fibromata contain cystic cavities, which arise from germ epithelium becoming cut off in the depths of the furrows. Such invaginated epithelium may undergo carcinomatous degeneration (fig. 64). Orthmann observed a case of this sort in a surface fibroma the size of a hazel-nut. The tumour consisted of numerous masses of large rounded and oval squamous epithelial cells, which here and there contained cystic cavities. Some of the cavities contained coagulated

FIG. 63.

PAPILLARY SURFACE FIBROMA OF THE OVARY.



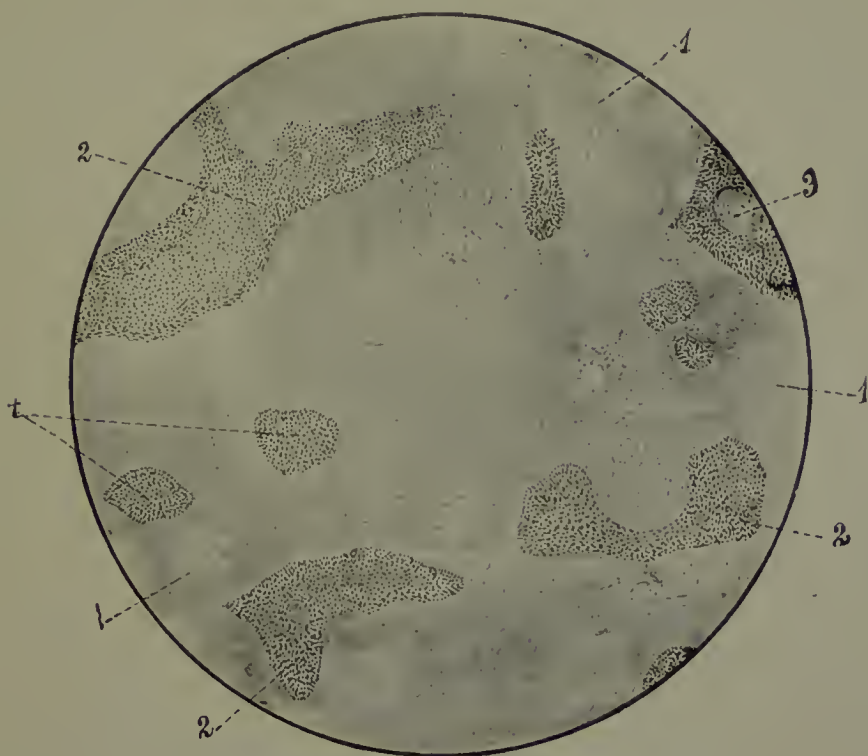
1. Surface fibroma, very poor in nuclei.
2. Outer covering of the ovary.

3. Germ epithelium.
4. Chalky concretions.

(Haematoxylin-eosin stain.)

FIG. 64.

SUPERFICIAL PAPILLARY FIBROMA OF THE OVARY UNDERGOING CARCINOMATOUS CHANGES.

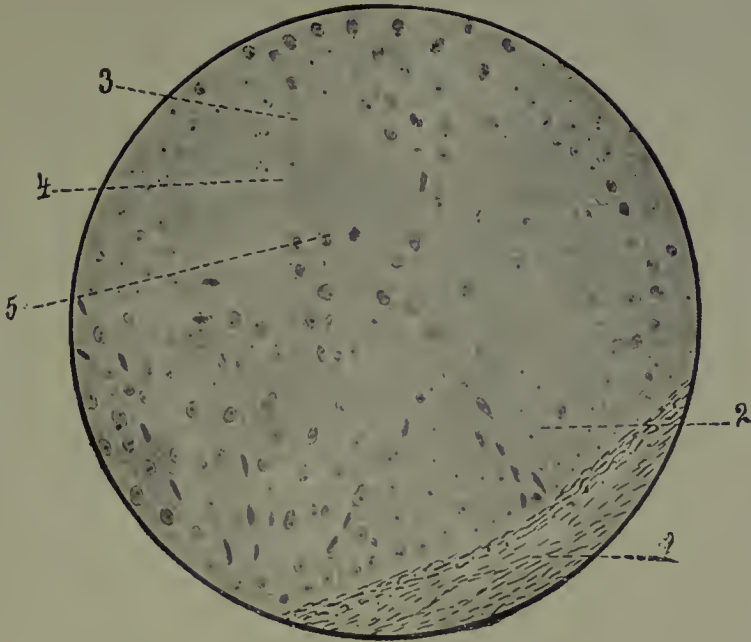


1. Fibrous connective-tissue stroma.
2. Solid epithelial nests and cones.
3. Cavity containing fibrin-coagulum within a group of epithelial cells.
4. Rounded epithelial cell-nest containing regularly arranged marginal cells.

(Haematoxylin-eosin stain.)

FIG. 65.

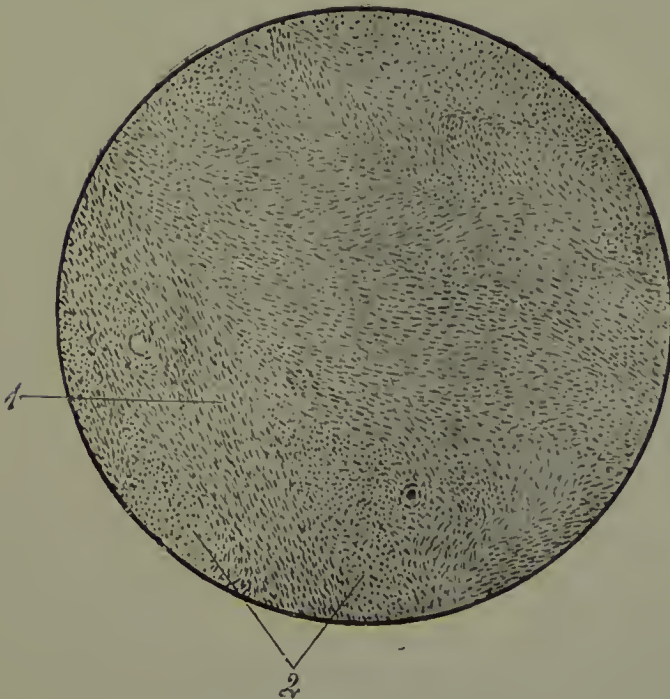
SUPERFICIAL PAPILLARY FIBROMA OF THE OVARY,
SHOWING CARCINOMATOUS CHANGES.



1. Fibrous connective tissue.
 2. Large squamous-like epithelial cells.
 3. Cylindrical epithelial cells lining a gland-like cavity.
 4. Fibrin coagulum.
 5. Vesicular cells resembling ova.
- (Hæmatoxylin-eosin stain.)

FIG. 66.

DIFFUSE FIBROMA OF THE OVARY.



1. Longitudinal section of fibrous bundles.
 2. Transverse section of fibrous bundles.
- (Van Gieson's stain.)

fibrin, others contained peculiar vesicular cells almost resembling ova (fig. 65). In the region of the pedicle similar epithelial groups in the ovarian tissue were found, which pointed to the growth being a primary carcinoma beginning in the surface epithelium.

(β) The diffuse or pure ovarian fibromata are usually unilateral, and vary in size from a walnut to that of a man's head. They are rounded or oval in shape, and in that respect often resemble a normal ovary. Their surface may be quite smooth, but here and there may exhibit nodular elevations. Their consistency is extraordinarily firm and dense, and on section they are composed of an interlacing network of tendon-like white fibrous tissue.

Among the secondary changes occurring in these tumours are œdematous infiltration combined with large areas of softening (fibroma lymphangiectodes, s. œdematosum), and myxomatous degeneration (myxo-fibroma). Ossification and calcification are rare.

More important still are fibromata showing definite adenomatous changes (adeno-fibromata). These growths have a porous appearance, and sometimes contain very large cystic cavities (cysto-fibromata). Carcinomatous and sarcomatous changes have also been noted in connection with these growths.

Microscopically the tumours consist of dense fibrous connective tissue bundles rich in cells, which interlace in all directions (fig. 66).

The softer fibromata contain a larger number of elements than the harder variety. Not uncommonly dilated lymph spaces and extensive lymphectatic cavities occur, combined with œdematous infiltration of the fibrous tissue. The latter must not be mistaken for true myxomatous degeneration.*

* A very useful distinguishing stain is hæmatoxylin, or double staining with thionin-toluidin. Œdematous tissue is

The adeno-fibromata have a fibrillary connective tissue stroma which is beset with numerous gland-like spaces; the latter are lined with a cylindrical or low cubical epithelium (fig. 67), and may sometimes form cysts of considerable size.

The adenomatous formations contained in fibromata may undergo either colloid or carcinomatous degeneration. In colloid degeneration isolated gland lumina are seen which are only partially lined with cylindrical epithelium, the remainder of the lumen being filled with a striated homogeneous material (fig. 68). Sometimes the epithelium completely disappears, and all that remains is a mass of colloid material (adeno-fibroma colloides).

(ii.) *Myo-fibroma and Myoma*.—Myo-fibromata of the ovary are rare, while pure myomata are still more uncommon. In ordinary fibromata, smooth muscular fibres have been sometimes observed. Pure myomata however do occur, and arise usually from the hilum or the region of the ligamentum ovarii. They may be either subserous or interstitial, and often displace the ovarian tissue before them, but remains of ovarian tissue in the capsule can often be clearly made out. Myomata of the ovary usually have a rounded somewhat nodular appearance, and may reach the size of a hen's egg or an apple.

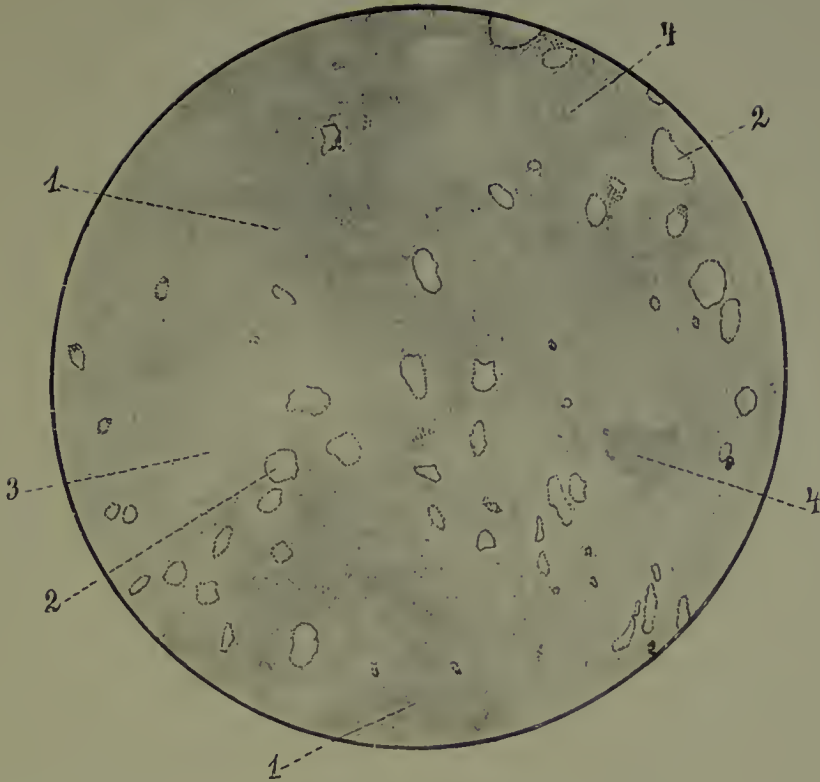
practically unstainable, while myxomatous and colloid material become uniformly blue with hæmatoxylin. Thionin-toluidin, a double stain (which unfortunately does not last long), brings out myxomatous or colloid material a clear violet, while the connective tissue and nuclei are stained bluish-green.

Technique of the thionin-toluidin staining method :—

- (1) Thionin concentrated watery solution : 3 to 5 minutes.
- (2) Wash in water.
- (3) Toluidin (2 drops of a concentrated watery solution, water 5 cc.) : 2 minutes.
- (4) Wash in water.
- (5) Absolute alcohol.
- (6) Origanum oil.
- (7) Canada balsam.

FIG. 67.

ADENO-FIBROMA OF THE OVARY.



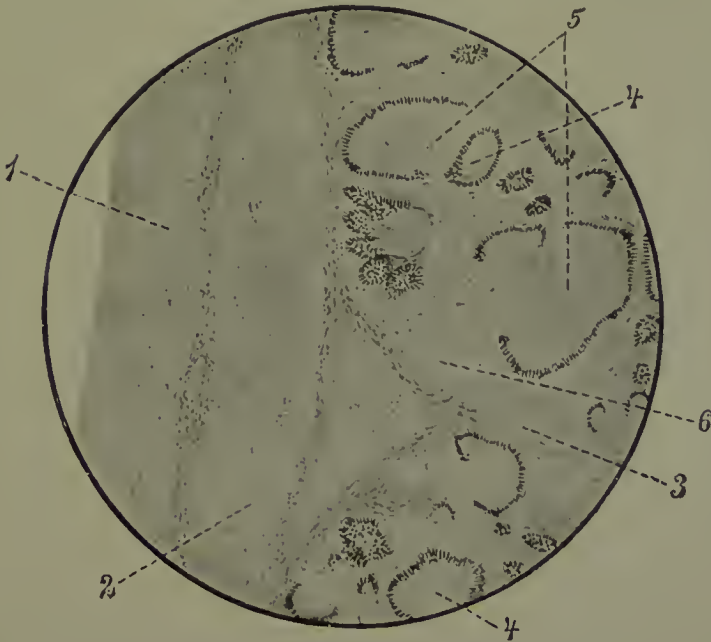
- 1. Fibrous connective tissue.
- 2. Gland-like spaces lined with low cubical epithelium

- 3. Connective tissue undergoing hyaline degeneration.
- 4. Chalky deposits.

(Hæmatoxylin-eosin stain.)

FIG. 68.

COLLOID ADENO-FIBROMA OF THE OVARY.



- 1. Fibrous capsule of the tumour.
- 2. Thin fibrillary connective tissue.
- 3. Dense fibrous connective tissue.
- 4. Gland-lumina, showing commencing colloid degeneration of the epithelium.

- 5. Gland cavities, showing more extensive degeneration.
- 6. Gland cavities distended with colloid material.

(Hæmatoxylin-eosin stain.)

Microscopically they consist of smooth interlacing muscular bundles, which are separated from one another by a certain amount of loose connective tissue. If treated by van Gieson's stain the characteristic difference between the muscular and connective tissue elements is very clearly displayed.

(b) MALIGNANT NEW GROWTHS.

(1) CARCINOMA OF THE OVARY.—Carcinoma of the ovary may occur either primarily or secondarily. The latter is especially seen with carcinoma of the uterus and Fallopian tubes, but it also occurs secondarily to cancer of the stomach, rectum, breast, &c. Carcinoma of the ovary may be either unilateral or bilateral.

Primary carcinoma of the ovary may arise from unaltered ovarian tissue, or it may occur in an ovary which has undergone cystic changes (carcinomatous degeneration of a cystic adenoma). The size of the tumours may vary from that of an apple to that of a man's head, their surface is often uneven and nodular, while the amount of cystic material as compared with the solid, varies considerably.

Numerous cystic spaces are found in the interior of primary carcinomata of the ovary. As a result of this their consistency varies greatly. The solid carcinomatous portions are usually distinguishable by their whitish-yellow marrow-like appearance.

Instead of the usual division of carcinomata into scirrhous and medullary, it is better to differentiate them according to their histological structure. Thus two principal types may be recognised, viz., glandular and papillary, these however often occur in combination with one another.

(i.) *Glandular Carcinoma*.—Glandular carcinoma may occur both as a primary cancer of the ovary, or as a cancerous degeneration of an adenomatous cyst. In the former case the direct origin of the new growth from

the superficial epithelium in early cases can easily be made out. The structure of this variety of carcinoma is decidedly alveolar.

The superficial epithelium forms gland-like invaginations into the stroma, which become cut off and form solid cones and nests as the result of epithelial proliferation.

The cells are principally squamous in type, but here and there they are seen to be cylindrical. The cell nests are usually solid, but sometimes cavities of variable size are found in their interior. These cavities contain fibrin coagula and vesicular cells somewhat resembling ova (fig. 65).

Carcinomata developing in glandular cysts have a similar structure, and arise from an atypical proliferation of the cyst epithelium. They usually grow either from the smaller cysts, or from epithelial tubes lying in the connective tissue walls of the larger cyst cavities.

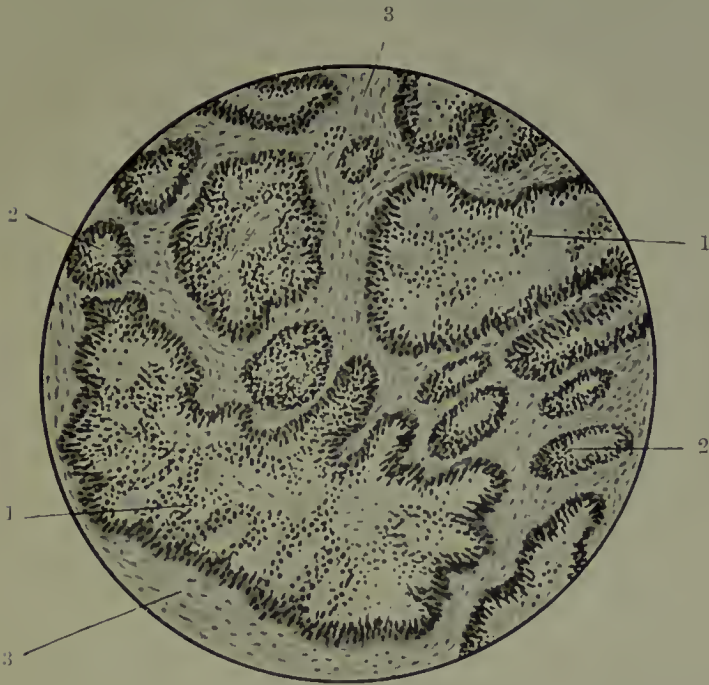
The tall cylindrical cells lining the carcinomatous alveoli become stratified or form papillary proliferations into the gland lumina, which gradually become filled with epithelial cells. Epithelial outgrowths may also be seen to extend into the stroma. Later, colloid or myxomatous degeneration of the cancer cells not infrequently occurs in the interior of the solid epithelial cell nests and cones. By this means secondary cavities are formed within the cancerous alveoli which were originally solid (fig. 69).

A peculiar form of glandular carcinoma is sometimes met with, characterised by the presence of numerous small cystic cavities within the cellular portion of the carcinomatous tissue. These cavities are lined by a regular layer of epithelium (cysto-carcinoma). In their immediate neighbourhood numerous epithelial tubes and cysts of different sizes are met with, distinguished by a commencing stratification of their epithelium.

On closer inspection the cancerous cell areas appear

FIG. 69.

GLANDULAR CARCINOMA OF THE OVARY.

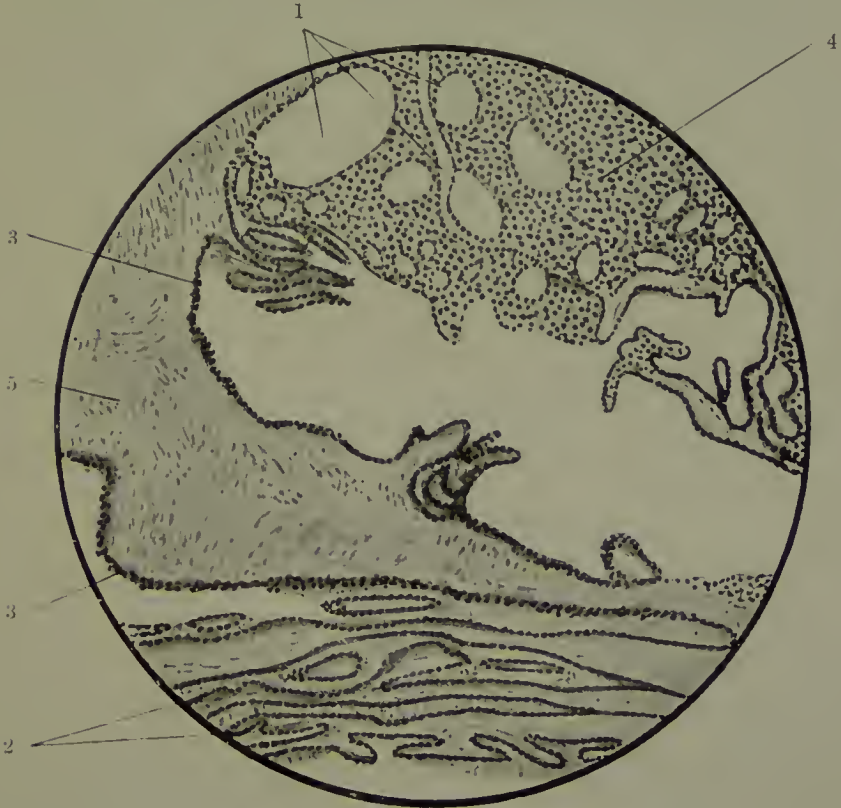


- | | |
|--|---|
| 1. Large glandular tubes, containing degenerated epithelium. | 2. Gland-lumina, containing many layers of cells. |
| 3. Loose interstitial connective tissue. | |

(Hæmatoxylin-eosin stain.)

FIG. 70.

CYSTIC GLANDULAR CARCINOMA OF THE OVARY.

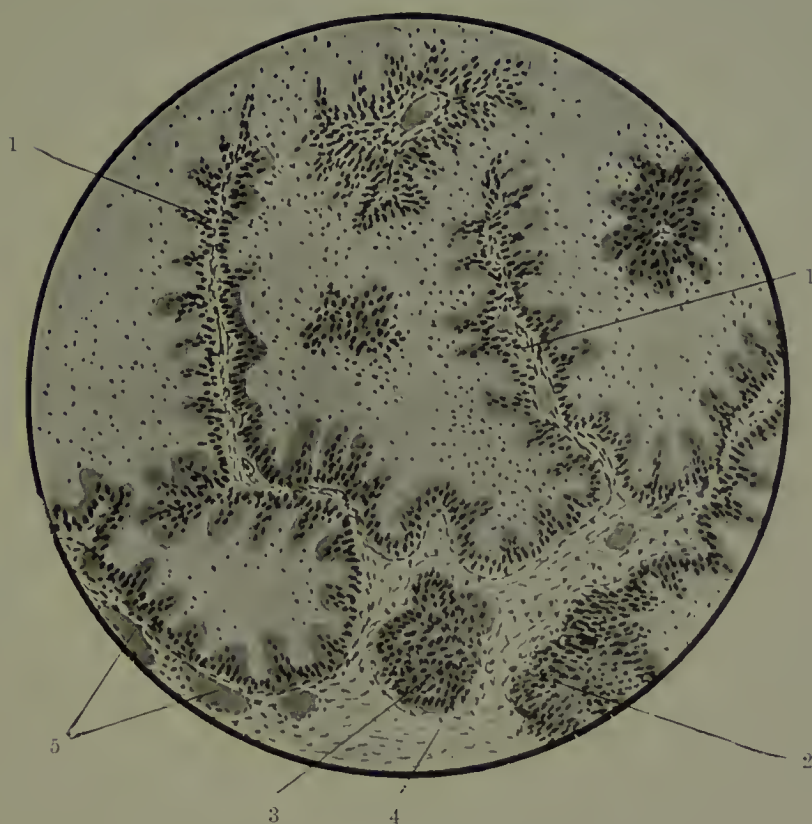


- | | |
|---|---|
| 1. Small cystic cavities amid the cancer cells. | 4. Cancerous tissue. |
| 2. Gland tubes, lined with single-layered epithelium of a low type. | 5. Interstitial tissue undergoing hyaline degeneration. |
| 3. Stratified epithelium. | |

(Hæmatoxylin-eosin stain.)

FIG. 71.

PAPILLARY ADENO-CARCINOMA OF THE OVARY.



1. Papillae, covered with many layers of epithelium.
2. Solid epithelial masses.
3. Isolated cancer alveoli.
4. Loose interstitial connective tissue.
5. Blood-vessels.

(Hæmatoxylin-eosin stain.)

to be made up of minute cysts, larger groups of which are separated from one another by delicate connective tissue septa (fig. 70).

(ii.) *Papillary Adeno-carcinoma*. — Papillary adenocarcinoma is relatively frequent; it always develops from a papillary adenomatous cyst, from which macroscopically it can hardly be distinguished. Malignancy may be suspected however when portions of very soft apparently solid marrow-like growth occur within the connective tissue wall of the cyst.

Microscopically the cylindrical epithelium covering the papillæ becomes at first many-layered and grows inwards towards the lumen of the cyst as well as into the wall itself. Thus solid epithelial cell nests and alveoli are formed; the former arise by constriction of the proliferating epithelial columns in the cyst wall, the latter by adhesion of the summits of the papillæ to one another (fig. 71).

The original tall cylindrical epithelium eventually assumes a cubical, squamous, or even polymorphous type.

Chalky concretions are found within the connective tissue septa as well as in the epithelial cells. This may occur to such an extent that the surface of the tumour feels quite gritty (psammo-carcinoma). Other secondary changes occur in the stroma such as myxomatous and colloid degeneration. Peritoneal metastases are frequently met with in carcinoma of the ovary.

(2) SARCOMA OF THE OVARY.—Sarcomata of the ovary occur much less frequently than carcinomata, but may attain a considerable size, even exceeding that of a man's head. They may be unilateral or bilateral, and are usually rounded or oval in shape. Their surface may be smooth or nodular, the separate nodules sometimes being only connected with the main tumour by a

thin pedicle. The growth usually has no capsule, the lobes of the tumour being visible upon the surface.

Sarcomatous tumours vary much in their consistency, this firstly depends on their histological structure (spindle-celled sarcomata being harder than round-celled sarcomata), secondly on the presence of numerous cystic cavities or hæmorrhagic areas of softening in their interior. On section, sarcomata are generally reddish-yellow in colour and have a homogeneous marrow-like appearance.

From a histological point of view two main varieties of ovarian sarcomata may be differentiated, viz., the round-celled sarcoma and the spindle-celled sarcoma.

(i.) *Round-celled Sarcoma*.—Round-celled sarcomata are rarer than the spindle-celled variety; they are much softer, more homogeneous and marrow-like on section, while their vascularity is also much greater.

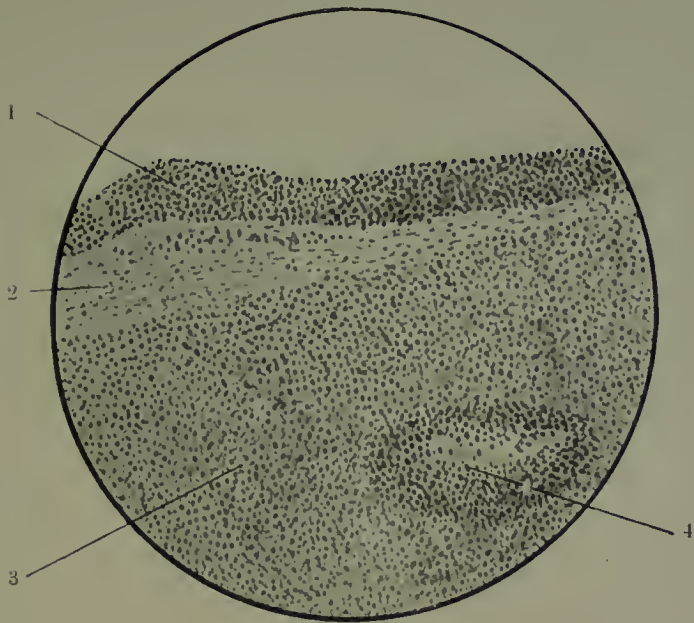
Microscopically, they consist of closely packed small round cells, the large nuclei of which stain deeply and are surrounded by clear protoplasm. Between the tumour cells a delicate connective tissue framework can be made out in which spindle-cells are discernible. The framework may sometimes give almost an alveolar appearance to the growth. Not infrequently lymphatic vessels crowded with round cells are met with in the stroma of the tumour. A broad layer of typical sarcoma cells is often seen on the peritoneal surface of these growths (fig. 72).

Round-celled sarcomata are exceedingly malignant and very early in their career give rise to metastases on the peritoneum and in neighbouring organs (tube, uterus, &c.).

(ii.) *Spindle-celled Sarcoma*.—Spindle-celled sarcomata are characterised macroscopically by a more fibrous structure than the round-celled variety, while their consistency is also much firmer.

FIG. 72.

ROUND-CELLED SARCOMA OF THE OVARY.



- 1. Peritoneal layer of sarcoma cells.
- 2. Remains of tunica albuginea.

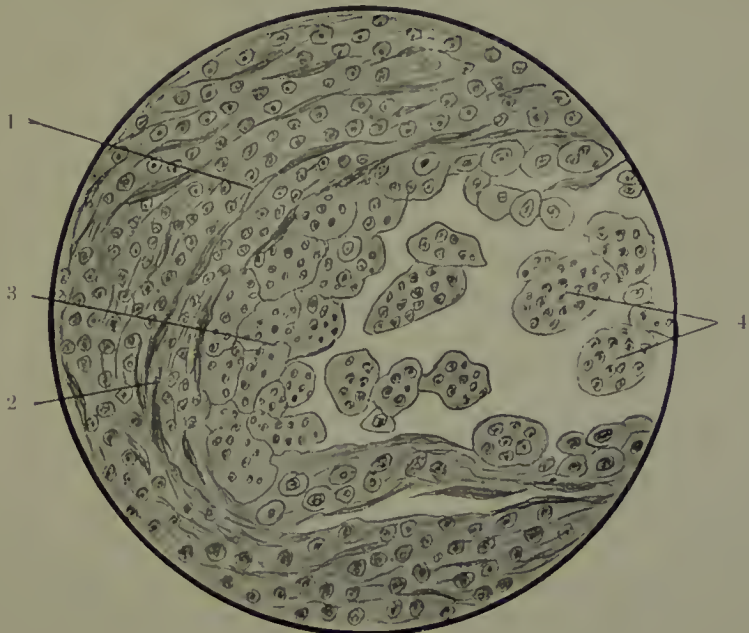
- 3. Small round-celled sarcoma cells.

- 4. Lymph vessel crowded with sarcoma cells.

(Hæmatoxylin-eosin stain.)

FIG. 73.

ENDOTHELIOMA LYMPHATICUM OF THE OVARY (SOMORSKI).



- 1. Tumour cells arranged like a string of pearls.

- 2. Spindle-shaped connective tissue cells.

- 3. Proliferation of the tumour cells lining an alveolus.

- 4. Giant-cells.

(Hæmatoxylin-eosin stain.)

Microscopically, they consist of numerous thick interlacing spindle cells which may be distinguished from fibroma cells in that they are found lying together in large groups and that they are much less uniform in character. The nuclei vary much in size and staining capacity, and are remarkable from the extraordinary amount of chromatin contents and asymmetrical nuclear division figures. The connective tissue framework is less marked than in round-celled sarcoma, and is usually poor in vessels.

(3) ENDOTHELIOMA AND PERITHELIOMA OF THE OVARY.—Endothelioma and perithelioma belong to the group of malignant connective tissue new growths having sarcomatous characters. From their naked-eye appearances they can hardly be distinguished from sarcoma, and often occur in combination with other tumours (cysts, embryomata, &c.).

Microscopically their structure shows some noteworthy characteristics, which will be shortly described.

(i.) *Endothelioma*.—Endotheliomata originate from the lining membrane of the blood-vessels (endothelioma vasculare) or the lymphatics (endothelioma lymphaticum).

In the earliest stages the endothelial cells of the vessels are considerably enlarged, they become thicker, more cubical or squamous in type, and may finally develop into well marked multi-nucleated giant cells. The cells at first grow amid the connective tissue bundles like a string of pearls and soon proliferate in tubular or cone-like masses in all directions, so that here and there a distinctly alveolar structure can be made out (fig. 73). In the later stages, so rapidly do the tumour cells proliferate that the interstitial tissue completely disappears and the irregularly placed cells now assume the appearance of a round-celled sarcoma.

(ii.) *Perithelioma*.—Perithelioma arises from the adventitia of the blood-vessels, possibly also from the peri-

vascular lymphatic spaces ; in the latter case it may be classed as an endothelioma lymphaticum.

Microscopically the structure of a perithelioma is very characteristic. In the neighbourhood of the existing vessels a thick zone of small round cells is seen ; this is more marked towards the lumen of the vessel, the inner wall of which is frequently seen to be undergoing hyaline degeneration. As a result of this curious grouping of the tumour cells around the lumen of the vessels the tumour frequently presents an alveolar structure. The individual groups of tumour cells are separated from one another by loose connective tissue. Finally, from these perivascular collections, strings of cells grow out into the surrounding stroma which is thickened and eventually becomes incorporated into the main mass of the growth.

In perithelioma, as well as in endothelioma, secondary changes occur as in ordinary sarcoma.

APPENDIX.

PAROVARIAN CYSTS.

In conclusion, a short description of parovarian cysts will be given. They may sometimes attain a considerable size. They are usually oval in shape and contain a thin watery fluid. They are always unilocular, and covered with a layer of thin moveable peritoneum. They arise from the parovarium or epoöphoron. Similar cysts may also occur in the broad ligament arising from accessory parovarian tubules.

Microscopically, three distinct layers may be seen in the cyst wall. The inner consists of ciliated cylindrical epithelium. The middle coat is made up of a thin stratum of wavy connective tissue usually poor in cells, and which sometimes contains smooth muscular fibres. Outside this is the loose connective tissue layer covered with characteristic peritoneal endothelium. Small papillary connective tissue outgrowths sometimes occur on the inner wall of such cysts.

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